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EDITORIAL

NEW SECTION BY THE ARMED FORCES AND PUBLIC HEALTH SERVICE

In recent years the contributions to the dental literature from career colleagues in the United States Armed Forces and the Federal health agencies have been voluminous and significant. In an effort to provide a consolidated and representative medium for these papers, the Editorial Board of the Journal has instituted a new section devoted to the United States Army, Navy, and Air Force and the United States Public Health Service. The chiefs of these services have been cooperative and enthusiastic in helping to establish this department. The excellent research opportunities and the volume and variability of clinical material in oral surgery, oral medicine, and oral pathology available to the Federal dental services should provide our subscribers with a wide scope of publications. The following have been appointed associate editors: Colonel Joseph L. Bernier, DC, USA; Captain Theodore A. Lesney, DC, USN; Colonel Donald C. Hudson, DC, USAF; and Dr. Edward J. Driscoll, United States Public Health Service. We look forward to a productive and mutually beneficial journalistic association.

In the March issue brief biographical sketches of these new associate editors will be presented.

I express my appreciation to Major General J. M. Epperly, United States Army; Rear Admiral C. W. Schantz, United States Navy; Brigadier General James S. Cathroe, United States Air Force; and John W. Knutson, Assistant Surgeon General, Chief Dental Officer, United States Public Health Service, for their assistance in bringing this new department into being.

K. H. T.

OPERATIVE ORAL SURGERY

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MALIGNANT LYMPHOMA OF THE MANDIBLE AND MAXILLARY REGION*

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DESPITE abundant literature concerning malignant lymphomas in general, little attention has been given tumors of this type affecting the mandible and the maxilla. We were able to find published descriptions of twenty-one such tumors in these locations, mostly as reports of single cases.[1-16] Malignant lymphomas in the facial region have been poorly understood and often misdiagnosed and wrongly treated.

PERTINENT LITERATURE AND CLASSIFICATION

For more than fifty years after Hodgkin published his original observation, no sharp distinction was made between lymphosarcoma and Hodgkin's disease, and the two were considered synonymous by the great majority of investigators.[17] In 1893 Kundrat[18] recorded fifty cases of lymphosarcoma and sought to differentiate it from Hodgkin's disease mainly on gross anatomic considerations. Sternberg,[19] in 1898, listed differential diagnostic points based on microscopic study. Dorothy Reed[20] accepted Sternberg's descriptions and agreed that Hodgkin's disease is an inflammatory granulomatous process.

After Reed, many accepted the view that a sharp line of demarcation existed between Hodgkin's disease and lymphosarcoma, but Gibbons[21] in 1906 and Coley[22] in 1907 believed that they were fundamentally similar. Oliver[23] added endothelioma to the group, thinking that it should be classed with Hodgkin's disease and lymphosarcoma. Mallory,[24] in 1914, proposed the term "malignant lymphoblastoma" to include lymphosarcoma, lymphatic leukemia, and Hodgkin's disease. Follicular lymphoma, or Brill-Symmers disease, was originally

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described by Becker[25] in 1901 but was not generally recognized as a separate type of tumor until the work of Brill and associates[26] in 1925 and Symmers[27] in 1927. Following this, in 1939, Parker and Jackson[12] described primary reticulum-cell sarcoma of bone.

For convenience, lymphoid tumors may be divided by histologic appearance into groups; however, these are not sharply defined, enduring, or mutually exclusive.[28] While some lymphoid tumors maintain the same histologic appearance throughout their course, others change. Warren,[28] Warthin,[29] and Custer and Bernhard[30] have suggested that the transition of one type of tumor into another indicates the histologic relationship among members of the group. It also explains the great confusion in classifying them.

After a consideration of all the classifications, the following one, modified from that of Nohlgren,[31] was employed in the current study:

1. Reticulum-cell sarcoma
2. Transitional type
3. Lymphosarcoma
4. Giant follicular lymphoma
5. Hodgkin's disease
    a. Paragranuloma
    b. Granuloma
    c. Sarcoma

The transitional type, with characteristics of both reticulum-cell sarcoma and lymphosarcoma, was added by us since many tumors present these borderline histologic features.

PRESENT STUDY

In a comprehensive review of small-cell lesions of the mandible and maxillary regions found in the files of the Mayo Clinic, eighty-two cases of possible malignant lymphomas with available histologic sections were found. Gross tissue was available for study in approximately 85 per cent of these cases, and in these instances new microscopic sections were prepared.

In the course of evaluation, nineteen of the eighty-two cases were discarded because they were not unequivocally malignant lymphomas. Also, twelve malignant lymphomas could not be used because of lack of proof of bone involvement, even though such involvement probably was present in most of them. Many of these twelve tumors were from the mandibular region, and on clinical examination they apparently were fixed to the jawbone; however, the radiologic and operative reports were not conclusive enough to warrant their inclusion in this series. The fifty-one cases left were studied thoroughly with respect to pathologic features, histories, roentgenograms, treatment, and course.

Careful review of the histories led to the discarding of four cases because lesions had been discovered in other parts of the body prior to the onset of symptoms of jaw involvement. One was first detected in an axillary node four

days before the jaw tumor was biopsied, and the other was found in a mesenteric node six years before the jaw lesion was noticed. These two lesions had been diagnosed as giant follicular lymphoma, but the later diagnosis of both was transitional-type lymphoma. The third case was discarded because enlarged cervical lymph nodes had been discovered six months prior to biopsy of the jaw tumor, although it is possible that the latter was primary. In the fourth case discarded, the patient had received treatment for a lymphoma involving the spinal cord about two months before the lesion of the mouth became apparent.

The remaining forty-seven tumors in this study were considered to be definitive primary lesions in the mandible or in the maxillary region. Thirty-four presented in the maxillary region, twelve in the mandible, and one in both bones. The group in the maxilla varied in the degree of invasion of the involved region. Many presented major involvement of the antrum, with or without prominent maxillary alveolar destruction. Frequently the walls of the maxillary antra were perforated by the tumors; in some cases several walls were perforated, so that swelling of the maxillary alveolar ridge or of the face, obstruction of the nose, or ocular proptosis occurred. Combination of these symptoms depended upon the degree of bony involvement. In spite of these differences, the tumors in the maxillary region were very similar clinically, and any subdivision on the basis of degree of bone involvement would have been merely arbitrary.

The roentgenograms from several of the earlier cases were not available, but the cases were included in the group because the clinical examination or the operative report definitely signified bony destruction. For example, a tumor causing bulging of the palate and over the antrum and resulting in proptosis of the eye was considered as definitely having osseous involvement.

TABLE I. HISTOLOGIC TYPES AND LOCATIONS

TYPES	TOTAL CASES	BONE INVOLVED		
		MAXILLA	MANDIBLE	BOTH
Transitional type	21	14	7	–
Reticulum-cell sarcoma	14	11	3	–
Lymphosarcoma	10	8	1	1
Hodgkin's disease	2	1	1	–
Totals	47	34	12	1

Of the forty-seven patients, twenty-two had no lymph nodes palpable on examination. The remaining twenty-five patients had cervical lymphadenopathy. In twenty-three of these the palpable nodes were restricted to the cervical region; the other two had enlarged nodes distant from those in the neck. The diseased nodes in all twenty-five cases were considered as probably secondary to the lesions of the jaws. In all forty-seven cases the chief reason for seeking treatment was the difficulty involving the mandible or the maxillary region.

After detailed histopathologic study, the forty-seven malignant lymphomas were classified as shown in Table I. The transitional type comprised 45 per

cent of the series and was the most common type in both jaws. The two patients with Hodgkin's disease had the granulomatous type of lymphoma. There were no giant follicular lymphomas.

The criteria for the histologic subclasses of malignant lymphoma as employed in this study are as follows:

Reticulum-cell sarcoma. The diagnostic feature of this tumor is its component of reticulum cells. These cells (Fig. 1, *a*) have an indented or lobulated nucleus, rather coarse chromatin, usually one or more nucleoli, and, ordinarily, indistinct cytoplasm.[10] The cells often are found in an alveolar arrangement, as in Fig. 1, *b*, with reticulin or collagenous fibers separating the cells into small clusters or rows.

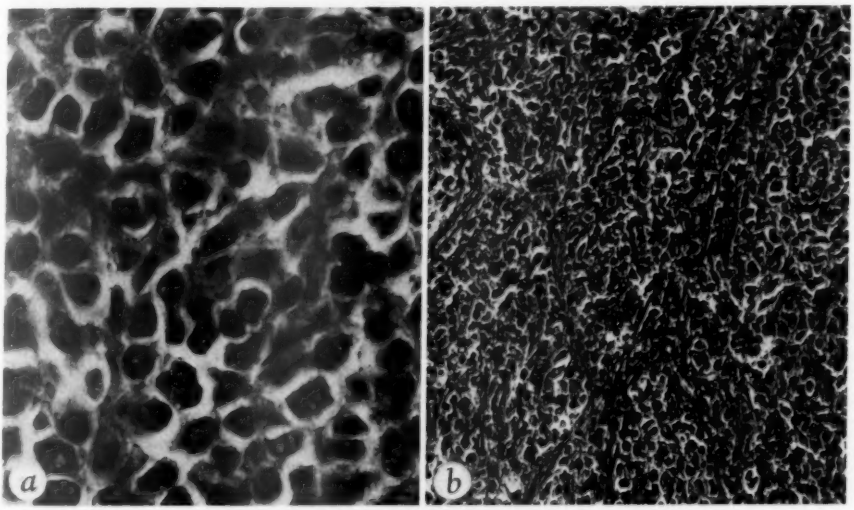

Fig. 1.—Reticulum-cell sarcoma. (Hematoxylin and eosin stain.) *a*, Characteristic lobulated nuclei and intercellular reticular framework. (Magnification, ×800.) *b*, Characteristic alveolar arrangement or clusters owing to the intercellular substance present. (Magnification, ×100.)

Lymphosarcoma. Lymphocytes of varying degrees of maturity[32] comprise this tumor (Fig. 2, *a*). The cells are uniformly round, with scanty basophilic cytoplasm, and the nucleus contains heavy masses of chromatin. The more immature cells may contain a visible nucleolus. Reticulin often is scanty. As with all malignant lymphomas, neighboring tissues commonly are invaded and destroyed to a variable degree.

Transitional type. The tumors that we have placed in this category show lymphocytes and reticulum cells of varying degrees of maturity (Fig. 2, *b*). The lymphocytes and reticulum cells may be present in approximately equal numbers, or either may dominate the picture. It seemed impracticable to attempt to set an arbitrary dividing line so that members of this transitional group could be assigned to the lymphocytic or reticulum-cell types.

Giant follicular lymphoma. Lymph nodes affected by this tumor have their normal architecture replaced by multiple follicle-like nodules of varied size and spacing.[33] They may be discrete or show partial coalescence. These nodules are present also in regions of extranodal invasion. The follicles are composed chiefly of reticulum cells, whereas the interfollicular areas are packed with lymphocytes.

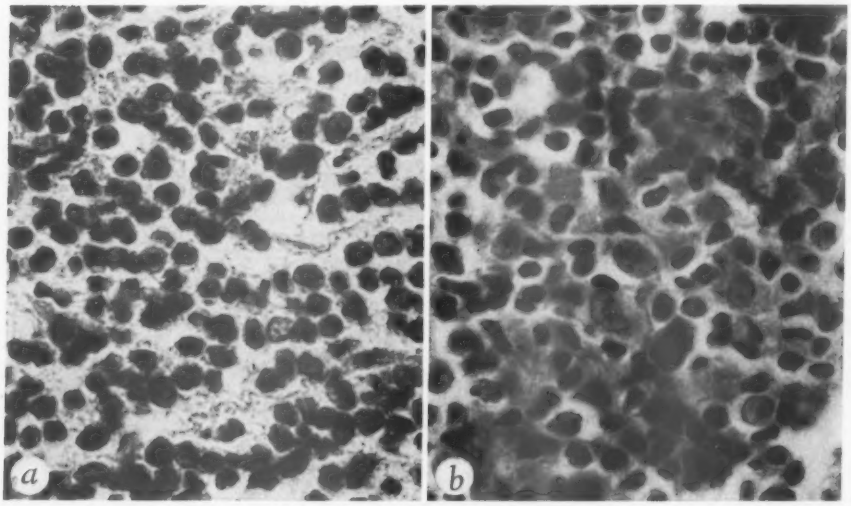

Fig. 2.—*a*, Lymphosarcoma, showing lymphocytes and lymphoblasts dominating the field. *b*, Transitional-cell type of malignant lymphoma showing a mixture of lymphocytes and reticulum cells. (Hematoxylin and eosin stain. (Magnification, ×800.)

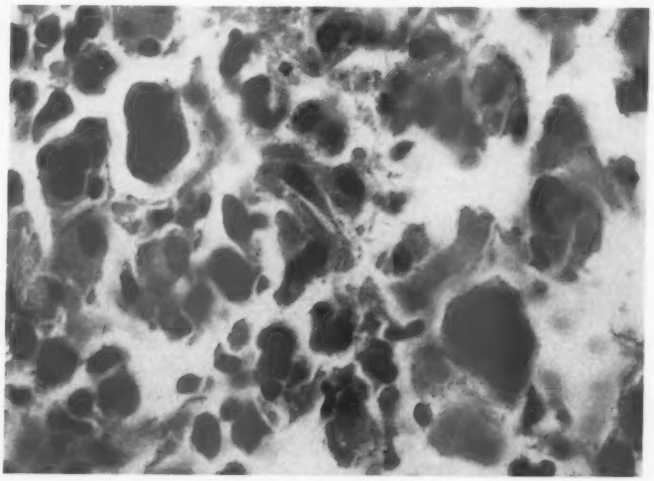

Fig. 3.—Malignant lymphoma of Hodgkin's type, illustrating giant (Sternberg-Reed) cells. (Hematoxylin and eosin stain. Magnification, ×800.)

Hodgkin's disease. This entity commonly is divided into paragranulomatous, granulomatous, and sarcomatous types.[32] The common denominator of the three is the Sternberg-Reed malignant giant cell (Fig. 3).

Paragranuloma. This most benign form of Hodgkin's disease is essentially an affection of the lymph nodes, particularly of the cervical region. For the most part, involved nodes are packed with fairly mature lymphocytes. The diagnosis depends on finding a few or many Sternberg-Reed cells. They vary from 12 to 40 microns in diameter and are irregularly shaped, with the cytoplasmic processes frequently extending between neighboring cells. Their nuclei are lobulated or multilobed, and hyperchromatic. Nucleoli, often multiple, may be either acidophilic or basophilic. Primary osseous involvement rarely, if ever, occurs in this type.

Granuloma. This most frequent form of Hodgkin's disease usually occurs in young adults. Again, the presence of Sternberg-Reed cells is diagnostic. Lymphocytes, lymphoblasts, eosinophils, plasma cells, and neutrophilic polymorphonuclear leukocytes are present also in variable numbers. Necrosis and fibrosis, features that enhance the similarity of this malignant tumor to an infectious granuloma, are common and may be extensive.

Sarcoma. This most malignant form of Hodgkin's disease has an aggressive, invasive nature and usually results soon in death. The tumor is composed of anaplastic reticulum cells, two to three times the size of normal lymphocytes. The nuclei are spherical and indented or ovoid and contain one or more prominent nucleoli. Mitosis is common, and Sternberg-Reed cells are present in varying numbers. Reticulin fibers usually can be demonstrated to enclose small groups of cells or individual cells.

DIFFERENTIAL DIAGNOSIS

Tumors were not included in the present series unless their component cells possessed the distinctive cytologic characteristics of lymphoma as detailed above. The basic cells varied from immature reticulum cells through the more mature forms, lymphoblasts and lymphocytes. As indicated, clear distinction between these component cells was not always possible. With rare exceptions, however, the members of the malignant lymphoma series could be distinguished readily from other small-cell lesions that affect the jaws. These include the following:

Ewing's tumor. Histologically, the almost complete lack of intercellular substance in large fields of this highly malignant neoplasm contrasts with the reticular framework or the residua of the invaded tissues lying between individual cells or small clusters of cells of the lymphomas. Cytologically, the nuclei in Ewing's tumor are round to oval, are more regular in size and shape, and have less clumping of chromatin than do the nuclei of the average lymphoma.

Myeloma. This neoplasm, like lymphoma, is of reticuloendothelial derivation. The salient difference is the large amount of discretely outlined cytoplasm so characteristic of myeloma cells even when immature. In the relatively rare highly undifferentiated myelomas, the nuclei lose their peripheral "cart-wheel" chromatin clumping and sometimes even their distinctive cytoplasm; such tumors may be difficult to differentiate from reticulum-cell sarcoma.

Reticuloendotheliosis (histiocytosis X). The histologically similar eosinophilic granuloma, Schüller-Christian disease, and Letterer-Siwe disease that comprise this group often affect the jaws. Differentiation from malignant lymphoma depends upon the lack of anaplasia among the differentiated histiocytes that make up the basic component of these disorders. Some of those unfamiliar with the histiocytosis X complex have been confused by the occasional mitotic figure that may be found among the proliferating histiocytes.

Inflammatory lesions. Lymphocytes, reticuloendothelial cells, and plasma cells, in varying combinations, may be so prominent in infections of the gingivae and jaws that there is a superficial resemblance to small-cell malignant tumors, especially lymphosarcoma and myeloma. The proliferating capillaries and fibroblasts, plus the cellular variety observed in inflammation, provide diagnostic clues. When one recalls, however, that secondary infection often complicates malignant lesions of the jaw, the problem is placed in true perspective. For biopsy, superficial tissue from an infected lesion obviously may be inadequate.

Epithelial lesions. Metastatic carcinoma and lymphoepithelioma contain cells that grow in clusters unlike the diffuse pattern of a lymphoma. The more discrete cytoplasmic margins and the lack of specific nuclear features of lymphoma also aid in differentiating these tumors.

Miscellaneous tumors. Rarely one may encounter other neoplasms that require differentiation from lymphoma in these locations. These include so-called esthesioneuroepitheliomas,[34] "retinal anlage" tumors,[35] and conventional neoplasms, such as osteogenic sarcomas, which may contain foci of small cells.

CLINICAL FEATURES AND COURSE

Sex and Age.—There were thirty-four male and thirteen female patients. Every histologic type affected both sexes, with no significant sex predilection in any type. The average age of the forty-seven patients at the time of admission was 46.8 years, and the median was 49 years (Table II).

TABLE II. DISTRIBUTION BY AGE AND TYPE (FORTY-SEVEN CASES)

AGE (YEARS)	TRANSITIONAL LYMPHOMA	RETICULUM-CELL SARCOMA	LYMPHO-SARCOMA	HODGKIN'S DISEASE	TOTALS
0-9	3	–	–	–	3
10-19	–	1	–	–	1
20-29	3	–	1	–	4
30-39	3	5	1	–	9
40-49	5	2	–	1	8
50-59	3	3	3	–	9
60-69	4	3	3	–	10
70-79	–	–	2	1	3

TABLE III. SIGNS AND SYMPTOMS (FORTY-SEVEN CASES)

	TRANSITIONAL LYMPHOMA	RETICULUM-CELL SARCOMA	LYMPHO-SARCOMA	HODGKIN'S DISEASE	TOTALS
Swelling	18	12	8	1	39
Pain	10	11	5	2	28
Lymphadenopathy	10	8	6	1	25
Ulceration	6	1	3	2	12
Nasal obstruction	5	3	4	–	12
Ocular proptosis	4	2	2	–	8
Numbness	3	2	2	–	7

Location.—As shown in Table I, thirty-four of these tumors involved the maxilla, twelve the mandible, and one apparently occurred in both bones, although osseous involvement was definite only in the maxilla. Twenty-seven of the thirty-four tumors of the maxilla presented to some degree in the antrum.

Signs and Symptoms.—The most significant clinical features of these malignant lymphomas are listed in Table III. Seventy per cent of the tumors were located so as to present some clinical feature intraorally. In swelling, the most frequent clinical finding, the masses varied from soft to hard and from diffuse to localized. Pain, experienced by twenty-eight patients, usually was described as "severe," "sore," or "aching." One patient with a mandibular tumor had pain only on opening the mouth.

Fig. 4.—Ulcer on lower right alveolar border, proved on biopsy to be due to transitional type of malignant lymphoma.

Lymphadenopathy, observed in twenty-five patients, involved the submaxillary and upper cervical nodes much more often than the other cervical nodes.

Intraoral ulceration was produced by eleven tumors, one of which had eroded through the nasal mucosa also. Another had ulceration in the nasal cavity only. Seven of the ulcers involved the alveolar mucosa, as shown in Fig. 4.

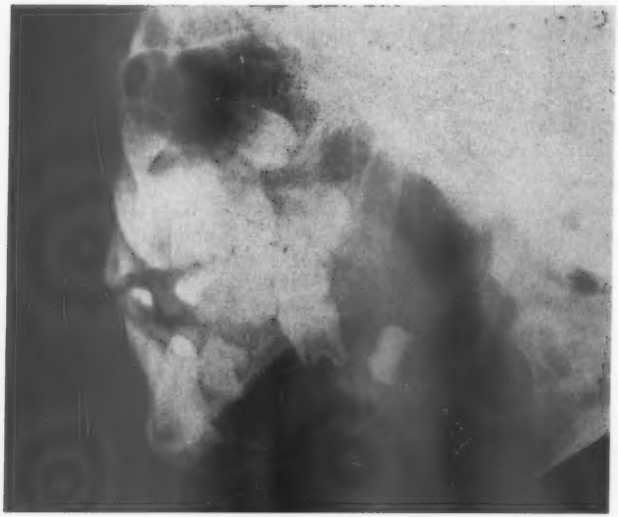

Fig. 5.—A destructive lesion in the mandible of a 6-year-old boy. Biopsy proved this to be a transitional type of lymphoma.

Fig. 6.—Hodgkin's granuloma of the right nasal fossa and antrum, showing destruction of the medial and inferior walls of the antrum. Carcinoma and other malignant lesions could produce a similar appearance.

Nasal obstruction occurred in twelve of the patients. In five of these the associated difficulty in breathing appeared to be the chief complaint, whereas in seven it was associated with other prominent symptoms. Ten of these patients had definite antral involvement.

Ocular proptosis, which affected eight, was unilateral in every instance and usually was associated with massive involvement of the maxillary sinus.

Numbness was noted by seven patients, of whom five had mandibular tumors. This anesthesia affected the mental region in two, the chin and lip in one, the chin alone in one, and the lip and lower teeth in one. Paresthesia was present in the cheeks of two patients, one of whom also had a numb upper lip.

The average duration of signs and symptoms for the entire group was 10.6 months, with variations from three weeks to ten years. The median was four months. Approximately 60 per cent had had symptoms for less than six months prior to admission to the Mayo Clinic.

Roentgenologic Findings.—Roentgenograms, or interpretations of them, were available in thirty-nine of the forty-seven cases in this series. Twenty-two of these showed destructive processes (Figs. 5 and 6). In the thirteen cases with roentgenographic evidence of involvement of the antrum only, the original descriptions ranged from "thickened membrane" to "increased density" to "diffuse opacity" of the antrum.

Treatment and Results.—The treatment given patients in this series was varied, as is specified in Table IV.

TABLE IV. TYPES OF TREATMENT (FORTY-SEVEN CASES)

TREATMENT	CASES
Radium	12
Roentgen therapy	11
Diathermy, radium	11
Radium, roentgen therapy	4
Diathermy, radium, roentgen therapy	2
Surgery, radium, roentgen therapy	2
Surgery, diathermy, radium	1
Diathermy, roentgen therapy	1
Roentgen therapy, surgery	1
Coley's serum	1
Biopsy alone	1

The term "diathermy" has been used to include electrocoagulation and cautery. Diathermy was utilized as an adjunct in fifteen cases.

The term "surgery" denotes procedures performed with a scalpel, chisel, saw, or rongeur. Surgery, other than biopsy and diathermy, was used in only four cases, and then in collaboration with other methods.

Radium, used more than any other mode of treatment, was employed for thirty-two patients, of whom twenty received other forms of therapy also. Roentgen therapy was given to twenty-one patients, of whom ten received other forms of treatment. Roentgen or radium therapy, or a combination of the two, was used in forty-five of the forty-seven cases.

We were able to determine the results of treatment in thirty-eight of the forty-seven cases in this series, nine having been lost to follow-up and of no value in determining results of treatment. One of the followed cases was not used in the statistics because of an unknown date of death. Another case with an indefinite date of death was used, however, because the patient was known to have lived at least three years following treatment.

Of thirty-six patients treated more than three years ago on whom follow-up data are available, thirteen are known to have lived at least three years. Of thirty-one patients treated more than five years ago on whom follow-up data are available, eight (26 per cent) are known to have lived at least five years. Of twenty-three patients treated more than ten years ago with adequate follow-up available, three are known to have lived at least ten years.

Radium or roentgen therapy was used alone or in combination in the treatment of all the patients surviving three or more years. Of the eight who are known to have survived more than five years after therapy, two had reticulum-cell sarcomas, one had a lymphosarcoma, and five had tumors of the transitional type. Only two of the eight five-year survivors were among the group with lymph node involvement.

Details regarding the postdismissal course of many of those patients who succumbed are not known. In one patient, however, leukemia was known to have developed. In five instances tumors developed at locations distant from the jaws. Two of these involved the soft tissue of the thigh, two involved the femur, and one involved the testicle and perineum. These tumors at distant sites developed at intervals that varied from three months to eight years following treatment of the jaw lesion.

ORIGINAL DIAGNOSIS

The majority of these patients originally had been considered to have some benign process, as evidenced by the treatment they had received. Twenty had had teeth extracted, twelve had had antral operations or treatment, and six had had incision and drainage. Various other ineffectual forms of therapy attested to the fact that the serious nature of their disease commonly was overlooked in its early stages.

COMMENT

Some may be critical of our including in this series all the malignant lymphomas that caused filling and destruction of the maxilla. In many instances, as we have indicated, proof of origin in the maxilla proper is not possible. Obviously, tumors located in the maxillary antrum and involving its walls may be of soft-tissue derivation. The clinical and pathologic sameness of these tumors, however, makes it impractical, if not impossible, to segregate a group in which there is overwhelming proof of origin in the maxilla proper.

This series illustrates the difficulty encountered when one attempts to pigeonhole members of the malignant lymphoma family into definite categories. The admixture of cell types led us to place 45 per cent of our cases in the

transitional category with features of both reticulum-cell sarcoma and lymphosarcoma. The subclasses of the malignant lymphomas presented no significant differences as to the region involved, clinical features, laboratory findings, roentgenologic manifestations, treatment, and prognosis.

Roentgenographic examination is helpful in delineating the region of involvement and usually suggesting that a malignant process is present. This study, like that of Wilson and Pugh,[36] indicates that the roentgenogram may strongly suggest or actually prove that the pathologic process is malignant, but it cannot be expected to disclose the histologic type. The diagnosis of malignant lymphoma depends on histopathologic study. The patient's complaint and the findings in the physical examination and the laboratory investigations are nonspecific.

It should be noted that a large percentage of the patients in this series had sought professional advice early in the course of the disease, only to be given inadequate therapy. Dentists and physicians alike should be alert to the probability that pain and swelling in the jaws, especially when associated with a destructive osseous lesion, may be due to a malignant bone tumor.

The biopsy, when an important lesion is suspected, should be performed by capable hands. The tissue obtained must have been deep enough that such factors as necrosis from previous treatment or infection cloud the issue to a minimal degree. As indicated previously, an important group of conditions must be considered in the differential diagnosis. One who is conversant with the problems of differential diagnosis and therapy is most likely to be successful in obtaining an adequate specimen for biopsy.

The vagaries of the malignant lymphomas are well demonstrated by this series. Patients with obvious, disseminated lymphoma may have a lesion in the jaws which appears clinically and roentgenographically to be primary. Accordingly, those with jaw lesions should be carefully studied for evidence of systemic disease. When attempting to evaluate prognosis, one must remember that patients with a localized malignant lymphoma may, at almost any later time, develop disseminated disease, a distant similar tumefaction or even leukemia.

Radiation is the mainstay in therapy of malignant lymphomas.[37] The philosophy of treatment is based on certain premises.[38] The first is that, like most other malignant tumors, most malignant lymphomas seem to begin in one place and spread from there, rather than arising as constitutional disease with multiple foci of origin. This suggests that localized instances should be treated aggressively in the hope of cure. The second premise is that, because they are extremely infiltrative, they are not usually suited to adequate surgical removal. The third premise is that, even when a fatality is inevitable because of the extent of the disease, remarkably effective and long control is sometimes possible.

Cures from the use of Coley's toxins, first reported in 1894, have been reported in some inoperable cases.[39]

The prognosis for malignant lymphomas localized to the jaws, with or without involvement of regional nodes, compares favorably with that for malignant

lymphoma primary in other sites.[40, 41] Approximately one-fourth of the patients can be expected to survive for five years, and this figure should improve if patients are accurately diagnosed and adequately treated earlier.

SUMMARY

In a study of malignant tumors of the maxilla and the mandible, forty-seven were found to have the histopathologic criteria necessary for the diagnosis of malignant lymphoma. The majority of these tumors involved the maxillary region.

There is commonly a prolonged delay in arriving at the correct diagnosis. In spite of this delay, an appreciable number of patients were saved by appropriate therapy.

This study indicates that, although it is important to recognize that a given tumor is a malignant lymphoma, further classification into the various types of malignant lymphoma is of small practical significance.

REFERENCES

1. Blum, Theodor, Kaletsky, Theodore, and Gettinger, Raymond: Agranulocytosis and Lymphosarcoma With Lesions in the Mandibular Third Molar Region, Arch. Clin. Oral Path. [Case Reports of the New York Institute of Clinical Oral Pathology] **4:** 378-383, 1940.
2. Burford, W. N., Ackerman, L. V., and Robinson, H. B. G.: Symposium on Twenty Cases of Benign and Malignant Lesions of the Oral Cavity: I. Lymphosarcoma in a Child, Am. J. Orthodontics & Oral Surg. **30:** 353-355, 1944.
3. Calman, H. I.: Lymphosarcoma of the Maxilla, ORAL SURG., ORAL MED. & ORAL PATH. **6:** 232-236, 1953.
4. Christiansen, G. W.: Lymphosarcoma of the Jaws and Palate, J. Am. Dent. A. **25:** 728-730, 1938.
5. Claman, Kenneth: Case Report: Lymphosarcoma of the Mandible, J. South California Dent. A. **20:** 22-23, 1952.
6. Fanale, S. J., and McCauley, H. B.: Lymphosarcoma of Dental Interest: Report of a Case, J. Oral Surg. **3:** 186-193, 1945.
7. Frank, V. H., and Pratt, C. I., Jr.: A Lymphosarcoma With Metastasis, J. Oral Surg. **9:** 19-24, 1951.
8. Gerry, R. G., and Williams, S. F.: Primary Reticulum-Cell Sarcoma of the Mandible, ORAL SURG., ORAL MED. & ORAL PATH. **8:** 568-581, 1955.
9. Harrigan, W. F., Butler, F. S., and Schaffer, A. B.: Reticulum Cell Sarcoma of Chin, J. Oral Surg. **12:** 210-214, 1954.
10. Ivins, J. C., and Dahlin, D. C.: Reticulum-Cell Sarcoma of Bone, J. Bone & Joint Surg. **35-A:** 835-842, 1953.
11. Khanolkar, V. R.: Reticulum Cell Sarcoma of Bone, Arch. Path. **46:** 467-476, 1948.
12. Parker, Frederic, Jr., and Jackson, Henry, Jr.: Primary Reticulum Cell Sarcoma of Bone, Surg. Gynec. & Obst. **68:** 45-53, 1939.
13. Penhale, K. W.: Primary Lymphosarcoma of the Mandible, J. Oral Surg. **1:** 84-88, 1943.
14. Seldin, H. M., Seldin, S. D., and Rakower, William: Oral Lymphosarcoma, J. Oral Surg. **12:** 3-15, 1954.
15. Szutu, Chan, and Hsieh, Chih-kuang: Primary Reticulum Cell Sarcoma of Bone: Report of Two Cases With Bone Regeneration Following Roentgenotherapy, Ann. Surg. **115:** 280-291, 1942.
16. Thoma, K. H., Holland, D. J., Jr., Woodbury, H. W., Burrow, J. G., and Sleeper, E. L.: IV. Contribution to the Oncology of the Jaws, ORAL SURG., ORAL MED. & ORAL PATH. **1:** 40-66, 1948.
17. Ginsburg, Solomon: Lymphosarcoma and Hodgkin's Disease: Biological Characteristics, Ann. Int. Med. **8:** 14-36, 1934.
18. Kundrat, Hans: Quoted by Ginsburg, Solomon.[17]
19. Sternberg, Carl: Quoted by Ginsburg, Solomon.[17]

20. Reed, Dorothy M.: On the Pathological Changes in Hodgkin's Disease, With Especial Reference to Its Relation to Tuberculosis, Johns Hopkins Hosp. Rep. **10:** 133-196, 1902.
21. Gibbons, H. W.: The Relation of Hodgkin's Disease to Lymphosarcoma, Am. J. M. Sc. **132:** 692-704, 1906.
22. Coley, W. B.: Hodgkin's Disease: A Type of Sarcoma, New York J. Med. **85:** 577-583, 1907.
23. Oliver, Jean: The Relation of Hodgkin's Disease to Lymphosarcoma and Endothelioma, J. M. Research **29:** 191-208, 1913.
24. Mallory, F. B.: The Principles of Pathologic Histology, Philadelphia, 1914, W. B. Saunders Company.
25. Becker, E.: Quoted by Brill, N. E., Baehr, George, and Rosenthal, Nathan.[26]
26. Brill, N. E., Baehr, George, and Rosenthal, Nathan: Generalized Giant Lymph Follicle Hyperplasia of Lymph Nodes and Spleen: A Hitherto Undescribed Type, J. A. M. A. **84:** 668-671, 1925.
27. Symmers, Douglas: Certain Clinical and Pathologic Aspects of Lymphosarcoma, Am. J. M. Sc. **174:** 9-29, 1927.
28. Warren, Shields: Histogenesis of Lymphoid Tumors, Acta Unio internat. contra cancrum (No. 3) **10:** 188-191, 1954.
29. Warthin, A. S.: The Genetic Neoplastic Relationships of Hodgkin's Disease, Aleukaemic and Leukaemic Lymphoblastoma, and Mycosis Fungoides, Ann. Surg. **93:** 153-161, 1931.
30. Custer, R. P., and Bernhard, W. G.: Interrelationship of Hodgkin's Disease and Other Lymphatic Tumors, Am. J. M. Sc. **216:** 625-642, 1948.
31. Nohlgren, J. E.: Current Concepts of Malignant Lymphomas: With a Study of 84 Cases, Portland Clin. Bull. **5:** 67-78, 1952.
32. Jackson, Henry, Jr., and Parker, Frederic, Jr.: Hodgkin's Disease and Allied Disorders, New York, 1947, Oxford University Press.
33. Gall, E. A., and Mallory, T. B.: Malignant Lymphoma: A Clinico-pathologic Survey of 618 Cases, Am. J. Path. **18:** 381-429, 1942.
34. McCormack, L. J., and Harris, H. E.: Neurogenic Tumors of the Nasal Fossa, J. A. M. A. **157:** 318-321, 1955.
35. Martin, Hayes, and Foote, F. W., Jr.: Third Case of So-called Retinal Anlage Tumor, Cancer **4:** 86-91, 1951.
36. Wilson, T. W., and Pugh, D. G.: Primary Reticulum-Cell Sarcoma of Bone, With Emphasis on Roentgen Aspects, Radiology **65:** 343-351, 1955.
37. Erich, J. B.: Discussion of Friedberg, S. A., Edwards, R. H., and Hass, G. M.: Malignant Lymphomas of the Pharynx, Tr. Am. Laryng. A. **78:** 85-89, 1957.
38. Craver, L. F.: Value of Early Diagnosis of Malignant Lymphomas and Leukemias, New York, 1952, American Cancer Society, Inc.
39. Coley, W. B.: The Treatment of Malignant Inoperable Tumors With the Mixed Toxins of Erysipelas and Bacillus Prodigiosus, Brussels, 1914, M. Weissenbruch, Printer to the King (Limited).
40. Bernatz, P. E.: Small Cell Neoplasms of the Stomach: A Clinicopathologic Study, Thesis, Graduate School, University of Minnesota, 1950.
41. Dawe, C. J.: Hodgkin's Disease and Its Interrelationships With Other Disorders, Thesis, Graduate School, University of Minnesota, 1955.

A FUNCTIONAL CEPHALOMETRIC RADIOGRAPHIC INVESTIGATION OF THE NASAL AND ORAL PHARYNGEAL STRUCTURES DURING DEGLUTITION IN OPERATED CLEFT PALATE AND NON-CLEFT PALATE PERSONS*

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DEGLUTITION, which the Swiss physiologist von Haller rightfully called the "difficillima particula physiologie," has aroused the interest of scientists since antiquity. Hippocrates (460-377 B.C.?), by vivisection of swine, came to the conclusion that a part of liquids swallowed go via the trachea into the lungs, to irrigate the pericardium to cool off the heart, and that the epiglottis acted as a guide, diverting as much of the liquids to the lungs as needed; the rest was to be channelled down to the esophagus.[1] In spite of the absurdity of this theory, it prevailed in the medical literature for 2,000 years. The first experimental physiologist, Erasistratus of Alexandria (about 300 B.C.), wrote a treatise on deglutition, in which he is said to have criticized Hippocrates. This treatise has been preserved only in quotations of other writers. Aristotle (384-322 B.C.) and Galen of Pergamum (A.D. 131-201) also discussed deglutition in their philosophic-medical writings. In ancient times the same subjects intrigued writers in the field, namely, the role played by the epiglottis and the nature of the peristalsis-like force which drives food from the mouth to the esophagus.

Magendie,[2] in 1817, wrote his classic description of deglutition in which he divided the process into three phases—the oral, the pharyngeal, and the esophageal—a division that later has been found appropriate by most authors describing swallowing. The first phase was described as voluntary, and the other two as involuntary.

In 1880 and 1883 Kronecker, Meltzer, and Falk,[3-5] employing a pressure measurement technique, concluded that the contraction of the mylohyoid muscle was the main force propelling the bolus and assigned to the constrictors only the functions of removal of residual food and closure of the glottis.

Discovery of roentgen rays in 1895 gave scientists a new and powerful tool, and it also opened a new era in the research of the physiology of deglutition. Cannon and Moser,[6] in 1898, introduced the use of the fluoroscopic screen and radiopaque bolus. This new method, with many subsequent improvements, led

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to the present-day techniques of lateral cephalometric radiography and cineradiography. Although these methods brought about a better understanding of swallowing, the points of controversy remained. In 1930 Barclay[7] reported that there was no evidence of muscular propulsion beyond the mouth. He held negative pressure, rather than the action of the pharyngeal musculature, responsible for transportation of the bolus. However, few researchers agreed with Barclay.

Within the last decade a number of high-speed cineradiographic investigations (sixty or more frames per second) have been made.[8-11] Detailed analyses of the chronology of the process of deglutition and observation of the action of the posterior pharyngeal wall, soft palate, larynx, and epiglottis have become possible. Ramsey and associates,[11] reporting on the findings of a cineradiographic examination of 300 persons, noted that the soft palate elevates ahead of the bolus to close off the nasopharynx. After the major part of the bolus has passed, the velum is pulled so far inferiorly that the uvula reaches the level of the glosso-epiglottic valleculae.

Among all the hypotheses on the force which transports food, Podvinec's[12] theory seems most original. He gave credit for bolus propulsion to compression of an air bubble that is present in the pharynx above the bolus.

The nature of velopharyngeal movement has been found to vary in different functions. Passavant[13] had stated in 1865 that the valving during speech is effected by the levators of the palate and the superior pharyngeal constrictors, while the valving of swallowing, gagging, and vomiting was strengthened considerably by the palatopharyngeus muscles.

Falkson,[14] after studying both deglutition and speech, asserted in 1880 that swallowing was the most important function of the pharynx and palate and that in swallowing the velopharyngeal valving was more complete than in other palatal functions. He agreed with Voltolini, who had compared this mechanism with that of the sphincter ani. In 1953 Bloomer[15] noted the much stronger type of valving seen in swallowing as compared with speech. He called attention to the "difference between the simple valve action in speech and the peristaltic-like waves during deglutition." Müller[16] reported in 1955 that there is a completely different principle of activity of velopharyngeal valving during deglutition and speech.

As a consequence of the anatomic deformity of the oropharyngeal structures of a person with cleft palate, their function deviates considerably from that of a person without cleft palate, particularly during speech. Ritchie[17] and Bzoch[18] are among those who have emphasized that one of the most important factors involved in the speech defects of children with operated cleft palate is the lack of mobility of the velum. Very little has been reported on the effect of the cleft palate deformity on deglutition. Ardran and Kemp[9] asserted that some persons with cleft palate exhibit a modified swallowing pattern, while others do not. Podvinec[12] stated that in subjects with cleft, paralytic, or scarred palates the defective function of deglutition can be compensated by a special position of the head and neck as well as by dexterity of the

action of the tongue. Thus, the compressed air bubble that is necessary for propulsion of the bolus is formed in the hypopharynx without normal palatal participation. Podvinec averred that food regurgitation rarely occurs in these persons. In 1954 he also noted that adults with cleft palate who had apparently normal patterns of deglutition seemed to swallow smaller portions, let the liquid flow into the pharynx, and, by the aid of the tongue, form a smaller compression chamber at a lower level than usual.[19]

The human body possesses functional adaptability to loss or injury to certain tissues and structures. An example is the pronounced activity seen in some persons with cleft palate in the area of Passavant's ridge, which is formed by the pterygopharyngeal portion of the superior pharyngeal constrictor. Negus[20] observed that even total removal of the tongue does not lead to inability to swallow, because of the compensating action of the cheeks and the floor of the mouth.

The purpose of these investigations was to observe and compare the movement of the nasal and oral pharyngeal structures in persons with operated cleft palate and in persons without cleft palate. Deglutition and phonation of the speech sound "p" were the functional performances used.

Both the cleft palate and the non-cleft palate samples were composed of twenty-five male subjects between the ages of 10 and 30 years. The mean age of each group was approximately 15 years. The cleft palate sample included unilateral and bilateral complete and incomplete clefts. No subjects with speech appliances were chosen, but many had received speech lessons. All those examined were patients at the Northwestern University Cleft Palate Institute, and the speech of each had been recently evaluated by the staff. The subjects without cleft palate possessed moderately good dental occlusions and were free of any recognizable oral deformity.

The method was lateral cephalometric radiography. Because of high kilovolt peak values, the x-rays produced have a high degree of penetration and allow a short exposure time. This is of special advantage in recording the rapid actions of deglutition and speech. The best soft tissue definition was obtained by using 200 Ma. and 90 KVP, and this setting was used with an exposure time of 1/20 second.

Differences in structural densities between the pharyngeal wall, tongue, and velum are not great enough to allow observation without a contrast medium. These structures were made radiopaque by the use of Iodochlorol (G. D. Searle & Company) and a paste of barium sulfate and gum tragacanth. Iodochlorol was applied through the left nostril, and the barium sulfate paste was applied to the oral structures. The head was stabilized in the cephalostat, with the Frankfort plane horizontal, by means of ear-rods and orbital positioners (Fig. 1).

Altogether, six exposures were made. Four were made while the subject was swallowing, at the time when the larynx was seen at its highest position (Figs. 2 and 5). One exposure was made during phonation of the plosive consonant "p" by repeating the syllable "pa" several times (Figs. 3 and 6). The sixth exposure was made with all structures at a position of rest or relaxation (Figs. 4 and 7).

The radiographs were developed by an observational technique for best soft tissue visualization.

The radiographs were placed on a transilluminated tracing table and the one representing the highest position of the velum during deglutition was selected for tracing. In a number of the subjects two or more of the radiographs of deglutition were identical. Of the radiographs representing the sound "p," only those which showed the lips closed were traced. A tracing was also made of the rest position radiograph.

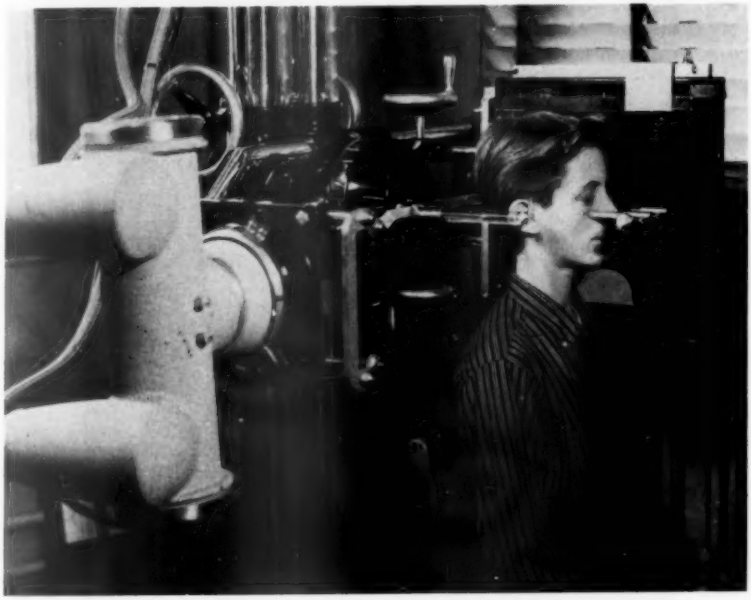

Fig. 1.—Cephalostat with subject oriented for lateral cephalometric radiograph.

The hard structures of the head and neck, as well as the outlines of the velum, tongue, and posterior pharyngeal wall, were traced. By superimposing the tracings of rest position, deglutition, and phonation of the consonant "p," a composite tracing was made for each subject (Figs. 8 to 11). The structures that had changed position during the functional performances were depicted by dotted and broken lines.

In spite of stabilization of the head during radiography, some movement of the head and cervical vertebrae could not be avoided. This was found to occur almost entirely at the atlanto-occipital joint, with the vertebrae acting as a unit. Consequently, the velum, tongue, hyoid bone, and mandible were traced while superimposed on the cranium, and the portion of the posterior pharyngeal wall which is attached to the vertebrae was traced while superimposed on the first four cervical vertebrae.

Fig. 2.

Fig. 3.

Fig. 2.—Lateral cephalometric radiograph of non-cleft palate subject with structures recorded during deglutition.

Fig. 3.—Lateral cephalometric radiograph of non-cleft palate subject with structures recorded during phonation of plosive consonant ("p").

Fig. 4.

Fig. 5.

Fig. 4.—Lateral cephalometric radiograph of non-cleft palate subject with structures recorded at nonfunctioning position.

Fig. 5.—Lateral cephalometric radiograph of cleft palate subject with structures recorded during deglutition.

Fig. 6.

Fig. 7.

Fig. 6.—Lateral cephalometric radiograph of cleft palate subject with structures recorded during phonation of plosive consonant ("p").

Fig. 7.—Lateral cephalometric radiograph of cleft palate subject with structures recorded at nonfunctioning position.

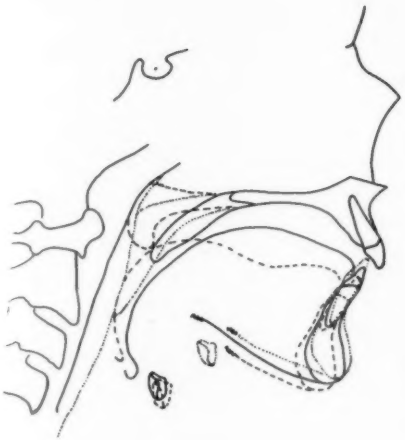

Fig. 8.

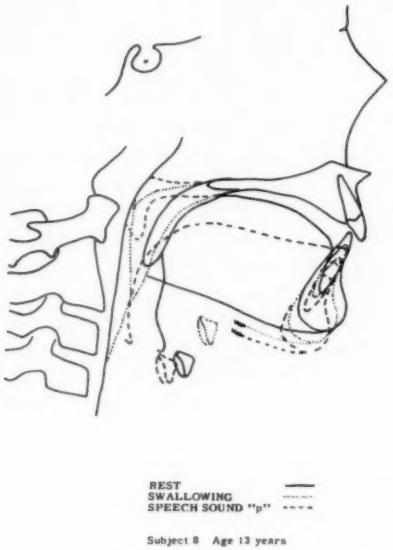

Fig. 9.

Figs. 8 and 9.—Typical composite tracings of non-cleft palate persons.

Fig. 10.

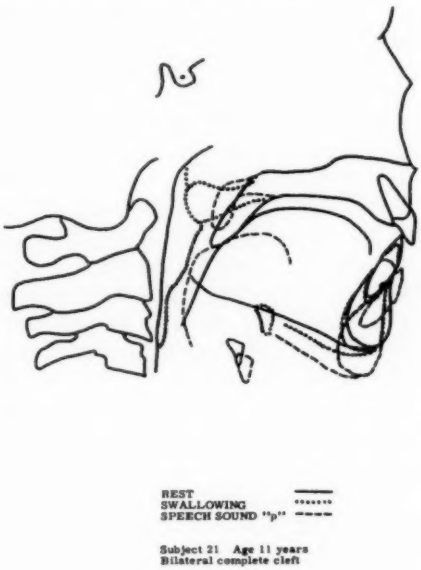

Fig. 11.

Figs. 10 and 11.—Typical composite tracings of cleft palate persons.

DISCUSSION

The original intention was to perform a study of deglutition in a manner similar to that of several previous studies in the field of speech, by expressing the positions and interrelationships of the involved structures through the use of numerical data and correlations. Such actions as posterior movement and elevation of the velum, pharyngeal activity, and movement of the hyoid bone and tongue would have been recorded as definite values. A careful analysis of five motion pictures[21-25] showing function of the pharyngeal and related structures, however, made it apparent that, using still radiography, detailed measurements would be of little value. The portion of the process of swallowing portrayed in one radiograph exposed for $\frac{1}{20}$ second reveals only a small fraction of a long and complicated physiologic procedure. It was also impossible to determine at what time in the act of deglutition the exposure had been made and to reproduce an identical stage of deglutition on different subjects. Furthermore, it was found that, because of the extreme speed with which swallowing takes place, the velum is in its highest position only a very brief instant and the likelihood of making exposure at this moment was very small.

Consequently, it was found that lateral cephalometric radiography has certain limitations as a means of studying deglutition. Roentgenocinematography would provide a method for a more complete, dynamic study of deglutition. By editing a film, frame by frame, one would be enabled to select a certain identical frame for each subject and then to make measurements and comparisons of this selected phase of the swallowing procedure. The investigations reported in this article show, however, that lateral cephalometric radiographs can reveal patterns of deglutition which are modified by structural deformity. Cephalometric radiography has other advantages also: the availability and lower cost of equipment, the relative ease of technique, the negligible radiation hazard, and the permanent records afforded for each person.

It seemed most practical to utilize an illustrative method, based on composite tracings of radiographs, as a means of displaying the findings of these investigations. The tracings for all of the fifty subjects are compiled in the original works, which are available in the Northwestern University Dental School Library. Samples of these composite tracings are portrayed in Figs. 8 through 11. The structures involved in the act of deglutition will be discussed individually.

The most striking difference between the cleft palate and non-cleft palate groups was seen in the behavior of the velum during deglutition. In both groups the velum moved superiorly and posteriorly to assist in closure of the velopharyngeal aperture. In the non-cleft palate subjects the velum often increased greatly in length and generally exhibited an arched configuration. In the cleft palate subjects the increase in length of the velum was small. The range of movement of the velum in these subjects seemed to be rather limited due to the shortness of the velum and its lack of mobility. In profile view, the velum showed relatively little arching and a thin and flat appearance.

The most superior point of contact between the velum and the posterior pharyngeal wall was situated at the approximate level of the anterior tubercle of the arch of the atlas, or somewhat above, in both groups. However, the most inferior point of this contact was much more inferiorly located in the noncleft palate subjects, usually at the level of the inferior border of the mandible or even below it, whereas in the cleft palate sample it was situated considerably above the inferior border of the mandible in all but two subjects. The distance between the most superior and inferior points of contact, that is, the length of the velopharyngeal contact, is shown in Table I. The average length was 40.24 mm. in the noncleft-palate group and 19.44 mm. in the cleft-palate group. These measurements only reveal a tendency toward a more effective velopharyngeal closure in persons without cleft palate during deglutition and do not carry significance as individual data, since the length of the velopharyngeal closure is constantly changing. A most important observation seems to be that even if the closure of the velopharyngeal valve during deglutition in the persons with cleft palate was short and probably light, there existed a complete closure in every subject. The shortness of the velopharyngeal contact in the cleft palate group may explain Podvinec's[19] observation that these patients have food entering the nasopharynx only when swallowing in the inverted position of Trendelenburg.

TABLE I. LENGTH OF CONTACT BETWEEN VELUM AND POSTERIOR PHARYNGEAL WALL

NON-CLEFT PALATE SUBJECTS		CLEFT PALATE SUBJECTS	
SUBJECT NO.	LENGTH OF CONTACT (MM.)	SUBJECT NO.	LENGTH OF CONTACT (MM.)
NFS 2*	24	15	8
4	25	2	11
6	27	5	13
21	30	21	15
14	31	23	15
11	33	8	16
23	33	10	16
7	36	11	16
25	36	25	16
12	37	22	17
16	37	1	18
8	38	3	18
13	41	12	18
17	41	20	18
5	43	4	20
3	44	16	20
15	45	17	21
20	45	6	22
1	46	7	22
24	46	24	24
10	49	14	25
19	51	19	26
9	53	9	27
18	53	18	30
22	62	13	34

Mean length of contact:
Non-cleft palate—40.24 mm.
Cleft palate—19.44 mm.

*Subject number in this investigation and in Normal Functional Series (NSF) at Northwestern University Cleft Palate Institute.

Ten successful radiographs were obtained of the phonation of the explosive consonant "p," in the cleft palate group and nineteen in the non-cleft palate group. These radiographs reveal very different conditions. The shape of the velum differed from that seen during deglutition. The velum can be described as hooked in appearance, the first third being parallel with the superior surface of the nasal floor or forming a small angle with it, the middle third in contact with the posterior pharyngeal wall at the level of the arch of the atlas or (in the majority of the subjects) above it, and the inferior part being curved away from the posterior pharyngeal wall. The length of the contact between the velum and the posterior pharyngeal wall was shorter than in deglutition, especially in the non-cleft palate subjects. These exhibited a complete closure in every instance, while only four of the cleft palate subjects showed a complete closure of the velopharyngeal aperture. Six cleft palate subjects had spacings of varying widths. Table II depicts the widths of the

TABLE II. WIDTH OF VELOPHARYNGEAL OPENING

NON-CLEFT PALATE SUBJECTS			CLEFT PALATE SUBJECTS		
SUBJECT NO.	DEGLUTITION (MM.)	SOUND ("P") (MM.)	SUBJECT NO.	DEGLUTITION (MM.)	SOUND ("P") (MM.)
2	0	–	1	0	–
3	0	–	2	0	–
9	0	–	3	0	–
11	0	–	4	0	–
21	0	–	5	0	–
23	0	–	6	0	–
1	0	0	7	0	–
4	0	0	8	0	–
5	0	0	9	0	–
6	0	0	10	0	–
7	0	0	11	0	–
8	0	0	12	0	–
10	0	0	13	0	–
12	0	0	14	0	–
13	0	0	15	0	–
14	0	0	16	0	0
15	0	0	17	0	0
16	0	0	18	0	0
17	0	0	19	0	0
18	0	0	24	0	1
19	0	0	20	0	8
20	0	0	22	0	8
22	0	0	25	0	10
24	0	0	23	0	12
25	0	0	21	0	15

velopharyngeal openings. The noticeable difference between the simple valve action of the velum during the function of consonant phonation and the more complicated action during the function of deglutition would suggest a more forceful and effective muscle action during deglutition than during speech.

The greater degree of velopharyngeal valving during deglutition shows the physiologic potential for full closure of the valve present in the muscles involved. Possible goals for muscle training in speech therapy are indicated for those cleft palate persons with insufficient velopharyngeal closure during speech. This finding harmonizes with the greater difficulty of many operated cleft palate subjects in mastering speech than in mastering deglutition.

In both groups, during deglutition, the tongue moved superiorly and posteriorly and was applied to the hard palate, velum, and posterior pharyngeal wall. An irregularly contoured dorsal surface of the tongue was seen in most of the cleft palate subjects, rather than the smoothly curved outline seen in the non-cleft palate subjects. This may be compensation for the shorter extent of the velum. The tongue shows its adaptability by conforming to the altered situation. It occupies the space normally filled by the velum and probably also takes over a part of the function of the propelling of the bolus of food, normally performed by the longer velum.

Contrary to what might be expected, the action of the posterior pharyngeal wall exhibited a similarity to an astonishing degree in both samples. Anterior movement of the posterior wall of the pharynx, which indicates function of the pharyngeal constrictor muscles, occurred in varying degrees in all the cleft palate subjects and in twenty-two of the non-cleft palate persons. The varying level and magnitude of this activity, as shown in the radiographs, could be interpreted as a momentary portrayal of the function of peristalsis in the musculature of the pharynx. This observation would indicate that action of the pharyngeal musculature is an integral part of deglutition, since no solid materials were swallowed and yet the peristalsis was stimulated into activity. The lack of pharyngeal movement in three of the non-cleft palate subjects corroborates the theory that considerable individual variations can be found in spite of the generally constant basic pattern during deglutition.

During phonation of the consonant "p," anterior movement of the posterior wall of the pharynx was observed in only two of the subjects with cleft palate and three of the subjects without cleft palate. In both groups this function was limited to the area of the ridge of Passavant at the level of or above the anterior arch of the atlas. The inactivity of the posterior pharyngeal wall during speech provides a dramatic contrast with the anterior movement seen during deglutition. The conclusion seems warranted that this muscle action is more effective and forceful during the function of deglutition than during speech.

The hyoid bone moved predominantly anteriorly and superiorly during deglutition, although there was a distribution throughout a range from pure anterior movement to pure superior movement. During phonation of "p," the amount of the movement of the hyoid bone was smaller and the direction was inconstant. The hyoid movement was similar in both cleft palate and non-cleft palate groups.

It was found on the radiographs that only fifteen of the subjects in each group swallowed with their teeth occluded. In ten subjects in each sample the teeth were slightly separated during deglutition. Swallowing with the teeth separated might represent a habitual pattern of deglutition for these persons, at least in the swallowing of liquids,[26] or it might be attributed to the unusual conditions during radiography.

Conclusions regarding movements of the head and cervical vertebrae did not seem to be warranted. As mentioned before, these movements occured in many subjects, and a compensation was made in superimposing during

the tracing procedure. Fixation of the subject into the cephalostat prevented natural movements but did not completely prevent incidental movements. The ear-rods unavoidably created an abnormal axis for head movement, situated above its normal site, the atlanto-occipital joint.

It was found, by correlating the closure of the velopharyngeal valve during phonation of the consonant "p" and by evaluation of speech adequacy done at the Northwestern University Cleft Palate Institute, that a positive relationship was indicated. The quality of speech became more inadequate, with respect to nasal emission and nasality, as the opening of the valve became larger. The small size of the sample makes statistical analysis of these data impractical, and a more detailed study of the relationships of these two factors would be desirable. The field of speech was not the main part of these investigations, and phonation of the sound "p" was added only to permit comparison of the velar and pharyngeal activity in deglutition with the activity involved in production of a typical speech sound.

It has to be taken into consideration in interpreting these data that only saliva with a small amount of the contrast medium was swallowed. This reveals the basic pattern of deglutition. The mechanism during swallowing of solid substances or larger amounts of liquids might vary from the basic pattern.

The following conclusions from these two investigations are suggested:

1. Muscle action in both cleft palate and non-cleft palate subjects was more effective and more forceful in the function of deglutition than in speech.

2. The velopharyngeal aperture was closed during deglutition in both cleft palate and non-cleft palate samples. During phonation of the consonant "p," the velopharyngeal aperture was closed in the entire non-cleft palate sample, but a number of subjects in the cleft palate sample exhibited openings of varying widths.

3. The shape of the velum differed during the functions of deglutition and phonation of the consonant "p" in both groups.

4. During deglutition the length of vertical velopharyngeal contact was markedly less in the cleft palate sample than in the non-cleft palate sample, since the velum did not extend as far inferiorly.

5. During deglutition the dorsal surface of the tongue exhibited a smoothly curved outline in the non-cleft palate subjects, while in the cleft palate subjects the outline of the tongue was irregular and inconstant.

6. Anterior movement of the posterior pharyngeal wall along its entire length was observed during deglutition, but during phonation of the consonant "p" the anterior movement occurred in few persons and was limited to the area of Passavant's ridge. Pharyngeal activity was similar in both groups.

7. The portion of the cleft palate sample in which phonation of the consonant "p" was radiographed showed a positive relationship between the width of the nasopharyngeal opening and speech adequacy as observed clinically.

REFERENCES

1. Eykman, P. H.: Der Schlingakt, dargestellt nach Bewegungsphotographien mittelst Röntgen-Strahlen, Pflüger's Arch. f. d. ges. Physiol. **99:** 513-571, 1903.
2. Magendie, F.: Précis élémentaire de physiologie, vol. 2, Paris, 1817, Mequignon-Marvis.
3. Kronecker, H., and Falk, F.: Über den Mechanismus der Schlundbewegung, Arch. f. Physiol. pp. 269-699, 1880.
4. Kronecker, H., and Meltzer, S.: Über die Vorgünge beim Schlucken, Arch. f. Physiol., pp. 446-447, 1880.
5. Kronecker, H., and Meltzer, S.: Der Schluckmechanismus, seine Erregung und seine Hemmung, Arch. f. Physiol., pp. 328-360, 1883.
6. Cannon, W. B., and Moser, A.: The Movements of the Food in the Esophagus, Am. J. Physiol. **1:** 435-444, 1898.
7. Barclay, A. E.: The Normal Mechanism of Swallowing, Brit J. Radiol. **3:** 534-546, 1930.
8. Saunders, J. B. deC., Cooper, Davis, and Miller, Earl R.: The Mechanism of Deglutition (Second Stage) as Revealed by Cineradiography, Ann. Otol., Rhin. & Laryng. **60:** 879-916, 1951.
9. Ardran, G. M., and Kemp, F. H.: A Radiographic Study of the Movements of the Tongue in Swallowing, D. Practitioner **5:** 252-263, 1955.
10. Rushmer, Robert F., and Hendron, John A.: The Act of Deglutition: A Cinefluorographic Study, J. Appl. Physiol. **3:** 622-630, 1951.
11. Ramsey, G. H., Watson, J. S., Gramiak, R., and Weinberg, S. A.: Cinefluorographic Analysis of the Mechanism of Swallowing, Radiology **64:** 498-518, 1955.
12. Podvinec, S.: The Physiology and Pathology of the Soft Palate, J. Laryng. & Otol. **66:** 452-461, 1952.
13. Passavant, Gustav: Ueber die Beseitigung der naeselnden Sprache bei angeborenen Spalten des harten und weichen Gaumens, Arch. klin. Chir. **6:** 333-349, 1865.
14. Falkson, R.: Beitrag zur Functionslehre des weichen Gaumens und des Pharynx, Virchow's Arch. f. path. Anat. **79:** 477-491, 1880.
15. Bloomer, Harlan: Observation on Palatopharyngeal Movements in Speech and Deglutition, J. Speech & Hearing Disorders **18:** 230-246, 1953.
16. Müller, E.: Zur Physiologie der Gaumensegelbewegung beim Schlucken und Sprechen, Arch. Ohren-, Nasen- u. Kehlkopfh. **167:** 472-477, 1955.
17. Ritchie, Wallace P.: Cleft Palate, a Correlation of Anatomic and Functional Results Following Operation, Arch. Surg. **35:** 548-570, 1937.
18. Bzoch, Kenneth R.: An Investigation of the Speech of Pre-School Cleft Palate Children, Ph. D. Thesis, Northwestern University, 1956.
19. Podvinec, S.: The Mechanism of Swallowing, Acta oto-laryng. **44:** 449-455, 1954.
20. Negus, V. E.: The Mechanism of Swallowing, J. Laryng. & Otol. **58:** 46-59, 1943.
21. Klatzky, Meyer: Physiology of Mastication (Assisted by W. H. Stewart), Lenox Hill Hospital, New York, 1939.
22. Ramsey, G. H., Watson, J. S., and Weinberg, S. A.: The Mechanism of Swallowing, Department of Radiology, School of Medicine and Dentistry, University of Rochester, 1953.
23. Ramsey, G. H., Watson, J. S., and Weinberg, S. A.: Demonstration of X-ray Findings in the Normal Pharynx, Department of Radiology, School of Medicine and Dentistry, University of Rochester, 1953.
24. Van den Berg, J. W.: Oesophageal Speech, Groningen, Holland, 1955.
25. Syrop, Harold M.: Intraoral and Pharyngeal Movements, Veterans' Administration Hospital, Chamblee, Georgia, 1951.
26. Rix, R. Ernest: Deglutition, Tr. European Orthodontic Society, pp. 191-202, 1948.

THE PROBLEM OF THE PREMAXILLA IN BILATERAL CLEFT LIP AND CLEFT PALATE

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THE cogent problem of the premaxilla in bilateral cleft lip and cleft palate, as related to occlusion, speech, and esthetics, varies in degree. The success of its correction is affected by the conditions that exist when the patient is first seen, the means available to control or improve them, and the patient's desire and ability to accept them.

The controlling factors may be categorized as anatomic and subjective, influencing the effect of the concerted efforts of the various disciplines upon the desired result. The diverse specialties involved in treatment preferably should be brought together as a centralized group clinic. This will permit the members of the team to make a regulated "on-the-spot" examination and evaluation, with free discussion, of the conditions and factors as they exist at a particular time. The various specialists are thus readily available to institute the phase or coordinated procedure that is indicated at any particular time.

A review of the embryology of the premaxilla recapitulates that following the fusion of the frontonasal process with the right and left maxillary processes, the free lower surface of the frontonasal process forms the premaxilla or primitive palate. The palatal processes appear in the sixth week; they grow from the maxillary processes mediad and fuse with the undersurface and posterior edge of the premaxilla in the eighth week. Bilateral cleft of the premaxilla would result from lack of fusion of these processes.

The objective of surgery is the formation of a firm and complete maxillary alveolar process of such contour that normal occlusion will be possible. Success in attaining this objective poses problems that require a knowledge of pre- and postnatal anatomy, physiology, and the forces of growth and development.

Failure of the frontonasal process to fuse with the lateral maxillary palatal processes permits an unrestrained anterior or ventral growth of the frontonasal process bearing the premaxilla. This projection can vary markedly in degree.

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The least degree occurs when both palatal processes have united with the base of the vomer to form a hard palate which is intact with the exception of a small triangular opening immediately posterior to the premaxilla. The premaxilla is in almost normal position and is practically immobilized by the fixation of the vomer to the hard palate. The surgical problem is merely the closure of the small triangular opening and the minimal alveolar clefts, usually by soft-tissue flaps.

In the more usual types, consisting of complete bilateral cleft of the palate and alveolar process, the projection of the premaxilla is marked, and the forces of growth and development during infancy tend to increase the amount of the projection, while the power of the buccinator muscles tends to force the mobile lateral segments inward until the ends of the alveolar processes may meet posterior to the premaxilla. The problem here is to place the premaxilla in as nearly normal a position as possible between the ends of the alveolar processes before they have been forced too far inward. The vomer begins as a portion of the cartilaginous septum of the nose and becomes enclosed by lateral plates of bone developing from centers of ossification near its lower edge. In the prenatal periods ossification has progressed until the lower edge of the septum has become completely enclosed in a bony covering which can be felt as a cylindrical rod connecting the free premaxilla with the bony posterior wall of the nasopharynx. The surgical problem is to shorten this rod sufficiently to allow the premaxilla to be placed in its normal position in the dental arch without directing its edge lingually. This can be done by removing a segment of the rod equal in length to the amount of projection of the premaxilla and cutting the cartilaginous septum above the point of removal vertically. The segment is removed near the posterior end of the septum; this solves the problem of lingual rotation, for the premaxilla can be set back in its normal vertical position.

Another problem is recurrence of the projection of the premaxilla due to formation of excess bony callus at the site of the excision. This problem is met by retaining the premaxilla in position by wire passing around the maxillary tuberosities—*not* by transalveolar wiring, which too frequently dislodges tooth buds. This procedure is more traumatic than closure of the lip, and the problem is met by developing the infant's resistance as rapidly as possible and operating as soon as satisfactory gain in weight has been obtained. In our experience, this time is indicated by a gain of 3 pounds above birth weight and the absence of oronasal infections.

The final surgical problem is stabilization of the premaxilla. This may be met in several ways. First, small mucoperiosteal flaps may be brought across the alveolar clefts from the anterior edges of the palatal plates to denuded bony surfaces of the premaxilla at the time of closure of the lip. Second, a mucoperiosteal flap may be reversed from the posterior surface of the premaxilla and held beneath the anterior ends of the mucoperiosteal flaps from the palatal processes with their raw surfaces in contact at the time of closure of the palate. (A long-term study of this method is now in progress.) Third, after a fairly large bridge of soft tissues has been formed across each alveolar cleft, the bridge may

be laid open, periosteal flaps raised from the sides of the alveolar cleft, the cleft packed with periosteal chips from any membranous bone (such as the rib), and the openings in the soft-tissue bridges closed over the chips. The success of this method requires stabilization of the sides of the clefts by orthodontic appliances during the period of development of the solid bony bridges; hence, this method will be used only after eruption of the teeth. The problem of preventing infection of the periosteal-chip bridge requires most careful aftercare.

Speech defects associated with abnormalities in the central segment of the upper dental arch are exclusively articulatory, and defective resonance is never a source of difficulty. Speech defects attributable to maxillary defects alone (excluding considerations of defects arising from any associated cleft of the velum and assuming that the patient is postoperative) will be confined to the fricative, affricative, and plosive sounds. While the general principles which apply can be enumerated with relative certainty, it is necessary to recognize that individual patients may show speech deviations in the presence of minimal maxillary deformity or have excellent speech in the face of gross deformity. This situation arises largely because of the fact that, within rather wide limits, there can be found compensatory lingual and labial movements or adjustments which result in acoustically good articulation. The reasons why one patient, without training, will make such compensation while another will not are not always fully understood.

In general, defective articulation results when the maxillary deformity and associated dental malocclusion make it difficult or impossible for the patient to create the necessary fricative or plosive sounds. Mention may be made first of the labial plosives *p* and *b;* for these, the lips must be brought together to impound the breath, which is then released to create a plosive sound. Any condition that interferes with such labial occlusion may, therefore, affect these sounds. Labiodental occlusion is a common substitute, but this may be undesirable from both a phonetic and an orthodontic point of view.

Certain of the speech sounds involve contact between the teeth and either the tongue or the lower lip. The sounds *f* and *v*, termed *labiodentals,* are made by placing the vermilion border of the lower lip in light contact with the incisal edge of the upper incisors; a friction noise is created when the breath is forced through this occlusion. Defective articulation may be the result of an edentulous area in the upper central area or of a relationship between the upper and lower arches which is so grossly abnormal as to interfere with labiodental contact. The *th* sounds (voiced and unvoiced) are linguodentals produced when the flattened tongue tip is placed in light contact with the incisal edge of the upper incisors or when the front of the tongue is flattened against their lingual surface. Therefore, these sounds are most commonly defective in edentulous patients, although there may be other easily recognized conditions in which the linguodental contact is difficult or virtually impossible.

Another group of sounds consisting of *s, z, sh,* and *zh,* often called *sibilants* or *linguo-alveolar* phonemes, requires that the breath stream be directed against the anterior part of the palate, the alveolar process of the premaxilla, and the

lingual surface of the upper incisors. Articulation difficulties on these sounds are very pervasive when the mouth structure is disturbed. When the patient is partially or completely edentulous in the upper central area, the friction sound sometimes cannot be created adequately. If the overjet is too great, an adequate friction sound is again impossible. Compensations may be effected by directing the breath posterior to its normal point or lateral to any abnormal opening in the bite. The affricates *ch* and *j* may be thought of as combinations of *t* and *sh* and *d* and *zh*, respectively, and hence will be affected as are *sh* and *zh* alone.

The most troublesome articulation difficulties arise in those cases in which, anteriorly, the mandible is prognathic. This occurs particularly as a characteristic in the patient with lip-jaw clefts, of course, where tongue size is disproportionately large in relation to the space remaining in the upper half of the oral cavity. Here the linguodental sounds are not likely to be affected, but the labiodental sounds may be. In line with the previous discussion, the sibilants may be thought of as *postdentals*, since the tip of the tongue must be adjusted behind the upper teeth. Hence, in cases of prognathism or maxillary deficiency, as is common in clefts, gross distortions of these sounds may result from the patient's inability to position the tip of his tongue behind the upper teeth. As a corollary, speech may be a secondary problem in prosthesis designed for masticatory function in cleft-palate cases, since often the postdental space is necessarily encroached upon. In all of these cases compensatory movements for speech characteristically prove very difficult.

The remainder of the plosive and fricative sounds present difficulties much less frequently. The plosives *k* and *g* require contact between the dorsum of the middle to posterior third of the tongue and that portion of the roof of the mouth immediately above. It is possible that extreme contraction of the upper arch might interfere with such contact, but it is doubtful that this will ever be seen clinically. The sounds *t* and *d* normally are made with the anterior part of the tongue in contact with the surface of the alveolar ridge behind the upper central incisors, but a satisfactory sound can be made with a more posterior contact. The sound *h* is a simple friction sound created by juxtaposing the vocal folds while breath is forced between them, while *wh* is a labial fricative sound not often affected by dental conditions. While no discussion of the point is necessary, it should be stressed that the same careful distinction must be made between *primary* and *secondary* speech defects in these cases, as will be mentioned in the discussion of velar insufficiency.

The dental phase may involve procedures in restorative dentistry, oral surgery, orthodontics, and prosthodontics. Teeth that are to be retained should be restored to health by means of the indicated replacement, including the amalgam or gold filling and the prefabricated or cast crown. At times one or more conditions may make it necessary to sacrifice one or more of the maxillary incisors. Some of the indications for this would be an abscess of the tooth, inadequate bony support, and malocclusion or displacement beyond the limits of orthodontics. In other instances, the premaxilla itself cannot be retroposed sufficiently, and thus is too far ventrad and/or protracted and must be reduced in bulk by

surgical intervention in order to permit the fabrication and insertion of a prosthesis. This decrease in dimensions may be in a vertical or a labial direction, or both.

Orthodontics comes into play when it is desirable or necessary to move individual teeth, groups of teeth, or segments of the arch into a position that will ensure greater ability to masticate, improve speech function and esthetics, or better position or contour the teeth for the retention of prosthetic appliances. Orthodontic appliances are also used in selected cases to open up the suture area that has been inhibited in its development by formation of excessive scar tissue.

Contraindications for orthodontic therapy are determined by the health of the teeth and the tissues supporting the teeth, the availability of bone in the area into which it is desired to move the teeth, and the number of remaining permanent teeth. The desirability of orthodontic care in any given case can be determined only after all the advantages and disadvantages of such therapy have been weighed against other types of therapy (namely, prosthetic restorations and corrective surgery) which may produce a similar result. Thus, in cases in which only minimal improvement would be attained by orthodontic therapy, other procedures are instituted.

The prosthesis, as its name implies, is an artificial device used to replace missing structures in the body. Its dental purpose is to emend the oral structures to the degree dictated by the factors controlling the prosthodontic treatment plan and appliance construction. In cleft-lip and cleft-palate prosthodontics, the prosthesis is essentially a removable partial or complete denture. Sometimes the planned fixed partial denture is used as an adjunct to the removable partial denture.

In addition to its being an aid to speech, the prosthesis is used to restore or improve the functions of mastication and gustatory pleasure and esthetics, with concomitant effects upon vocation and morale. The order of importance of these functions will vary with the individual patient, but it is obvious that improved speech and esthetics are greatly desired by most patients or their parents.

The design of the appliance is influenced by the anatomic structure and relationship of the premaxilla. Thus, the number of teeth remaining and the position of the premaxilla as related to the maxillae—that is, normal, retracted, or protracted—would be examples.

Continuous tooth contact is incorporated into the design of the major connector to provide the features of a retainer plate if these are needed. This would prevent relapse in cases in which there had been expansion of the arches as well as movement of the teeth.

The maxillary prosthesis indicated at a particular time for habilitation of the patient would include one of the following:

1. Space maintainer.
2. Temporary or primary type of appliance, with or without lip plumper.
3. Permanent type of appliance, with or without lip plumper.

4. Speech appliance incorporating a velar bulb, with or without a lip plumper.
5. Modified obturators, sometimes used with auxiliaries.

When the maxillary incisors are missing, the patient's growth potential will determine whether a temporary type or a permanent definitive type of appliance is to be fabricated. If replacement or modification will be required at various intervals because the child is in a phase of active growth, or if the patient is in need of a transient appliance during stages of surgery, the temporary type usually made of plastic with wrought wire clasps is indicated. The permanent type of appliance is fabricated when growth has become stabilized; it is of gold or chrome alloy combined with plastic. If a patient presents with a retruded lip or a collapsed underslung vermilion lip area, a plumper is added to the appliance to restore contour to the degree permitted by cicatricial attachment and length and width of the lip. The plumper may also act as a scaffolding for subsequent plastic revision of the lip.

In some postsurgical cleft-palate patients there exists a velar insufficiency per se or one due to the removal of portions of the tonsillar ring. Disorders of speech function associated with velar insufficiency can be classified into two categories: (1) defects arising from faulty resonance of the speech sounds and (2) articulation defects that result from insufficient intraoral breath pressure.

A brief explanation of the functioning of the velum palatinum in speech is necessary. In all voiced sounds in speech, the vocal note produced by the vocal folds within the larynx is resonated or reinforced in the cavities of the throat and head, particularly the pharynx, oral cavity, nasopharynx, and nasal passages. If the soft palate is relaxed so that the opening between the oropharynx and the nasopharynx is patent, the acoustic result is a vocal tone which the listener perceives as having a *nasal* quality or timbre. On the other hand, if the soft palate and other components of the velopharyngeal sphincter mechanism are contracted so that little or no breath passes into the nasopharynx and nasal passages, the resonance properties of the cavities are such that the tone has *orality*, or an absence of nasal resonance.

The same action of the velopharyngeal sphincters is needed for fidelity in a major group of English speech sounds which may roughly be classified as the consonants. Acousticaly, these sounds are produced as characteristic patterns of fricative and plosive "noises" created when the breath stream is directed, with adequate pressure, against various soft and hard surfaces within the mouth. The tongue and lip posture or movement that molds the breath stream is, of course, a neuromuscular pattern which is distinctive for each of the speech sounds, or *phonemes*. Faulty velopharyngeal function which prevents the development of adequate intraoral breath pressure will, therefore, make the normal articulation of these sounds difficult or impossible for the patient.

More specifically, resonance defects or conspicuously unpleasant voice quality may be noted on all voiced speech sounds except the three *nasals* of English speech. These latter sounds are those commonly spelled with the letters *m, n,*

and *ng* (as is *m*an, *no*, and si*ng*), although it should be noted that many words spelled with *n* have the *ng* sound, as in i*n*k or thi*n*k. Nasal resonance is normal in the three English nasals (and in other nasal sounds in languages other than English), but it is minimal or absent in other voiced speech sounds. In general, undesirable nasal quality will be most obtrusive on the vowels, dipthongs, and certain semivowels (*l* as in *look*, *y* as in *you*, *r* as in *run*, and *w* as in *we*). These sounds are identified by the listener on the basis of their resonance properties, and intraoral breath pressure is not a major consideration.

Roentgenographic and other studies show that velopharyngeal closure must be complete, or nearly so, if an undesirable degree of nasal resonance is to be avoided. On the other hand, judgments as to what constitutes excessive nasality are highly subjective and, from a practical point of view, a substantial amount of such resonance can be tolerated without handicapping the patient if the articulation is otherwise good. The examiner must be aware, also, that a vocal quality which commonly is identified as nasal may arise from sources other than velar insufficiency. Without going into detail, the quality termed nasality is the result of cul-de-sac resonance (in which a relatively small air-filled resonator is coupled to one of greater size), and certain abnormal tongue postures and constrictions of pharyngeal musculature may lead to the same acoustic end result as faulty velopharyngeal closure. This latter consideration must always be borne in mind, of course, when the patient's speech is being evaluated.

Defects of articulation based on insufficient intraoral breath pressure are typically much more conspicuous. Sounds likely to be involved are (1) *fricatives*, (2) *affricates*, and (3) *plosives*. The fricatives, produced by breath friction against a hard or soft mouth surface, are (to give common spellings) *s* as in *see*, *z* as in *zero*, *sh* as in *shoe* (the preceding group may be called *sibilants*), *th* as in *think* (unvoiced), *th* as in *that* (voiced), *f* as in *fat*, *v* as in *very*, *h* as in *hot*, and *wh* as in *what*. The affricates, which phonetically are combined *fricative-plosive* sounds, are *ch* as in *chicken*, and *j* or *g* as in *judge* or *gesture*. The plosives are *p* as in *pat*, *b* as in *boy*, *t* as in *to*, *d* as in *do*, *k* as in *keep*, and *g* as in *go*. Of the foregoing, the following are produced without voice: *s*, *sh*, *f*, one of the *th* sounds, *h*, *wh*, *ch*, *p*, *t*, and *k*; the remainder, being voiced, may be defective in both resonance and breath pressure. It might be suggested that, because of the inconsistencies in English spelling, the examiner should train himself to think strictly in terms of the sounds that he actually hears.

The *primary* result of poor velopharyngeal closure, and hence inadequate intraoral breath pressure, will be underarticulation of the fricative, affricative, and plosive sounds and an adversely conspicuous friction noise as the breath, obstructed by the tongue or lips, escapes through the nose. At the same time, cognizance must be taken of the fact that in typical individual patients the most obtrusive speech deviations may be *secondary*, or only indirectly related to inadequate velopharyngeal closure. Unfortuately, attention must be called to the fact that many young patients with cleft palate have defects which would have been present in any case, such as persistence of infantile speech, but which are mistaken for primary cleft-palate errors. Again, an indirect result of velar

insufficiency may be that the patient distorts sounds by producing them in nonstandard ways or fails to attempt certain sounds; presumably these faulty patterns arise unconsciously because of difficulty which the child experiences in developing normal speech sounds. Of great clinical importance is the fact that a high proportion of patients with velar clefts also have hearing losses which interfere with speech learning. Often there are conspicuous accessory facial grimaces, probably intended to be compensatory, associated with speech. Finally, emotional factors influencing the communicative process are frequently of the utmost importance.

Clinically, therefore, the speech evaluation must break down the defects of resonance and articulation errors due to inadequate breath pressure and must further define carefully the primary and secondary defects and their admixture. There is reason to fear that on occasion surgical and dental measures intended to improve speech prove of little avail because of failure to make such analysis. Likewise, poor speech may obtain when surgical and dental techniques have been entirely adequate, and this is very frequently the case.

As the earlier discussion implies, the speech criteria for adequacy of velar function is that it be capable of contributing its normal physiologic function to the process of velopharyngeal closure. This latter, of course, consists of backward and upward movement of the velum palatinum, combined with sphincteric action of certain pharyngeal muscles. The sources of poor postoperative velar function are well known: inadequate length and insufficient movement caused by functional weakness, immobility due to cicatrization or excessive tension and, very rarely, apparent interference with nerve supply.

When one is faced with a patient having *primary* speech errors related to velar inadequacy, the choices in procedure are limited. In some instances in which the palate is of moderate length and mobile, compensatory action of the pharyngeal muscles can be developed. Muscle training is always the first recourse when functional weakness is suspected. When the palate is short but mobile, or potentially so, a retropositioning operation or other secondary surgery, such as the pharyngeal flap, may provide an improved base for speech function. A speech prosthesis is always an alternative in such cases. When the palate is immobile because of cicatrization or tension, secondary surgery is not usualy indicated (excepting possibly the pharyngeal flap), and a speech prosthesis is more often a better choice. At all times, of course, there must be a realistic appraisal of how much improvement in speech function is actually needed and of whether or not the anticipated gain justifies the projected surgical or dental procedure where speech is the sole consideration.

When further surgical correction is contraindicated, a velar bulb is used. This artificial replacement of the missing musculature is constructed to the degree necessary to complete the velopharyngeal valving. At our clinic we use the plastic fixed type. This enables the inadequate speech pattern to meet functional requirements for speech production.

Occasionally, some patients present at our clinic with defects of the hard palate in the region of the premaxilla in conjunction with or without maxillary

teeth. When there is a problem of retention or leverage, the design of the prosthesis must be modified. It may be necessary to obturate the palatal hiatus and (if the speech is within broad acceptable limits) to omit the velar bulb in order to eliminate its lever action upon the anterior portion of the appliance. In other cases, auxiliary springs are used in conjunction with a mandibular appliance to provide retention when the other factors for its development are inadequate. After the appliance is inserted, it is not a catholicon. Adjustments and corrections may be required.

CONCLUSIONS

Patients presenting with clefts involving the premaxilla require the combined planned efforts of the various disciplines of a cleft-lip and cleft-palate team. The habilitation procedure at different periods may involve plastic surgery, speech therapy, orthodontics, oral surgery, restorative dentistry, or prosthodontics. The treatment plan at any phase should attempt to augment that of another phase that may be indicated later; therefore, it must be long range in scope.

REFERENCES

1. Baker, Herbert Koepp: Pathomorphology of Cleft Palate and Cleft Lip, in Travis, Lee (editor): Handbook of Speech Pathology, New York, 1957, Appleton-Century-Crofts, Inc., pp. 570-596.
2. Baker, Herbert Koepp: Speech Problems of the Person With Cleft Palate and Cleft Lip, in Travis, Lee (editor): Handbook of Speech Pathology, New York, 1957, Appleton-Century-Crofts, Inc., pp. 597-607.
3. Beder, O. E., Miller, W. J., Smith, G. P., and Ziskin, D. E.: Correction of a Cleft Palate Using a Stress-Breaker Type Partial Appliance With Obturator Attached, Am. J. Orthodontics & Oral Surg. **31**: 377, 1945.
4. Beder, O. E., and Saporito, L. A.: The Orofacial Cripple, Am. J. Orthodontics & Oral Surg. **32**: 351, 1946.
5. Beder, O. E., Bruno, S. A., Kaplan, J. I., and Lane, S. L.: Lip Plumpers, ORAL SURG., ORAL MED. & ORAL PATH., **1**: 1266, 1952.
6. Berry, M. F., and Eisenson, Jon.: Speech Disorders, New York, 1957, Appleton-Century-Crofts, Inc., pp. 305-351.
7. Bill, A. H., Jr., Moore, A. W., and Coe, H. E.: The Time of Choice for Repair of Cleft Palate in Relation to the Type of Surgical Repair and Its Effect on Bony Growth of the Face, Plast. & Reconstruct. Surg. **18**: 469, 1956.
8. Bloomer, H.: Speech Defects Associated With Dental Abnormalities and Malocclusions, in Travis, Lee (editor): Handbook of Speech Pathology, New York, 1957, Appleton-Century-Crofts, Inc., pp. 608-652.
9. Coe, Herbert E.: Cleft Lip and Cleft Palate, Surg. Clin. North America **36**: 1583, 1956.
10. Fymbo, L. H.: The Relation of Malocclusion of the Teeth to Defects of Speech, Arch. Speech **1**: 204-207, 1936.
11. McDonald, E. T.: Speech Considerations in Cleft Palate Prosthesis, J. Pros. Dent. **1**: 629-637, 1951.
12. McDonald, E. T., and Baker, Herbert K.: Cleft Palate Speech and Intergration of Research and Clinical Observation, J. Speech & Hearing Dis. **16**: 9-20, 1951.
13. Morley, M. E.: Cleft Palate and Speech, Baltimore, 1946, Williams & Wilkins Company.

SURGICAL EXCISION OF MINIATURE SIALOLITHS IN WHARTON'S DUCT

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THE surgical approach to the extirpation of small sialoliths in Wharton's duct can be fraught with difficulty for the unsuspecting surgeon. The ease with which larger concretions are removed has often led to a feeling of false security on the part of the operator. Nevertheless, the surgical eradication of single or multiple diminutive stones most assuredly presents difficulties. Therefore, it is the aim of this article to set forth a simple, rational surgical technique for the treatment of small nonpalpable salivary stones obstructing the submaxillary duct.

The clinical symptomatology, related pathology, and possible sequelae of sialoliths involving Wharton's duct have been thoroughly discussed in the literature. Neither the diagnosis nor the preoperative and postoperative management of such conditions presents serious problems to the practitioner. The major challenge to be surmounted is one of localization. The enigma results from the fact that the floor of the mouth is a three-dimensional, highly mobile operative area lacking the benefits of fixed anatomic landmarks.

Except as a means of demonstrating the presence or absence of calcifications, roentgenography is of little aid. The occlusal roentgenogram is limited in value for several reasons. The roentgen film is merely a flat plate and consequently lacks the quality of depth perception. Furthermore, there are no normal radiopaque structures in the floor of the mouth to which the position of a stone can be accurately related. Use of this x-ray view to pinpoint the object in question, is probably misleading to the observer, for at this time the mouth is closed and the tongue is depressed. The radiographic position of the stone relative to existing teeth and/or the medial aspect of the body of the mandible is certainly altered during surgery when the mouth is open, the tongue is deflected, and the oral floor is raised.

The one and only constant factor is that the calcification remains either completely or partially within the confines of the submaxillary duct. Therefore, with the exception of anteroposterior displacement, if the sialolith does move, it will do so only in conjunction with the duct. Herein lies the basis for the proposed procedure. The aim is to dissect Wharton's structure, isolate

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it, and subsequently remove the stone or stones. This can be accomplished by immobilizing that portion of the oral floor and duct to be exposed, confining the limits of the stone anteroposteriorly, and dissecting out the duct rather than blindly searching a maze of mobile soft tissue for the elusive stone.

PROCEDURE

The immobilization of the operative site as well as the confinement of the stone is accomplished by the placement of two deep sutures, one anterior and one posterior to the calcification. The sutures can be accurately inserted if they are made radiopaque by impregnation with an iodinized oil and then their position is checked with an occlusal film.

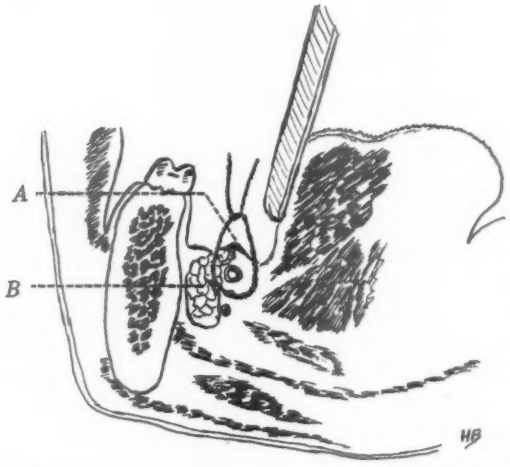

Fig. 1.—Cross section of anterior floor of mouth demonstrating the relationship of the plica sublingualis (*A*) to the sublingual gland (*B*). Note position of suture ligature placed around Wharton's duct.

Two anatomic features of the area can be exploited in circumscribing the duct. The plica sublingualis is an elevated crest of mucous membrane caused by the oral projection of the sublingual gland and is located in the floor of the mouth along the lateral border of the tongue posterior to the lingual frenum.[1] It can be utilized as a guide, since it closely approximates the anteroposterior course of the duct and is located in a plane directly above or slightly lateral to the pathway of Wharton's duct (Fig. 1). Secondly, since the duct progressively ascends as it courses anteriorly from the gland to its orifice,[2] the depth to which the suture must be placed can be readily reckoned (Fig. 2).

Once the anterior suture has been inserted, it is a simple matter to estimate the position for the posterior ligature. The rear suture is tied tightly to prevent the stone from slipping posteriorly while the forward suture may be only loosely applied. By keeping the sutures of sufficient length, it is possible to

grasp them manually, thus raising the operative site and making it taut. In addition, extraoral pressure under the floor of the mouth will aid in elevation of the area that is to be surgically explored. The sutures and the external compression facilitate a more accurate and simple dissection of the area.

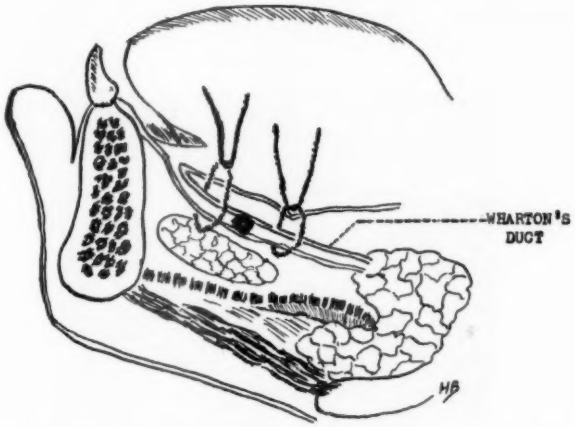

Fig. 2.—Longitudinal sketch of floor of mouth portraying ascent of Wharton's duct.

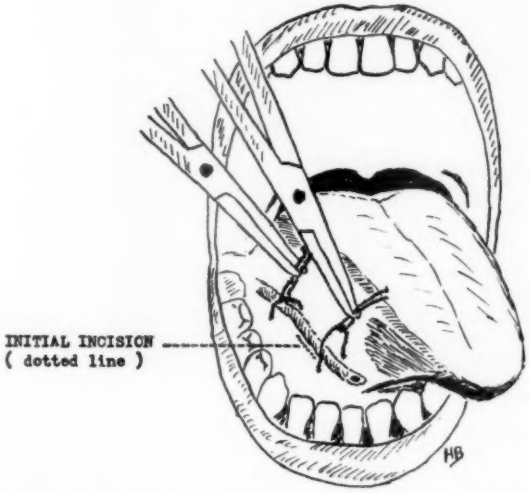

Fig. 3.—Intraoral sketch of oral floor demarcating initial incision line.

After these preliminaries have been accomplished, an incision through the mucous membrane is begun along the anterior aspect of the suture-demarcated operative zone. Here the duct is relatively superficial in relation to the mucous membrane of the floor of the mouth. The incision is made lateral and parallel

to the plica. A lateral approach has the advantage of offering better visibility and access without interference from the tongue (Fig. 3). Furthermore, it eliminates the hazard of encountering any strategic anatomic structures other than the sublingual gland. Anatomically, there are no major vessels or nerves present between the major portion of the submaxillary duct and the medial surface of the mandible.

Fig. 4.

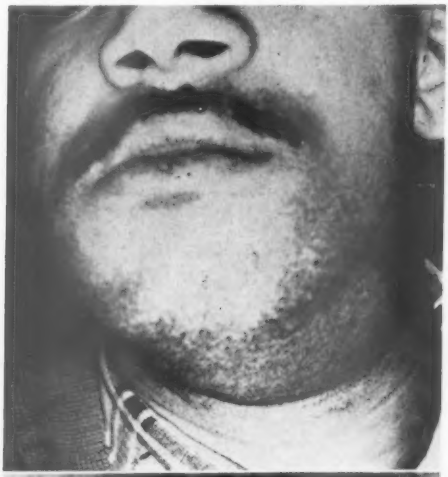

Fig. 5.

Fig. 4.—Extraoral appearance. Note swelling of left submaxillary and submental area.
Fig. 5.—Intraoral appearance demonstrating sublingual swelling.

Initial localization of Wharton's duct is obtained by means of blunt dissection. Subsequent to this primary ductal visualization, the incision is lengthened posteriorly to the rear suture and the remaining involved portion of the submaxillary duct is isolated via further blunt dissection. It then becomes a relatively simple matter to remove any stone or stones located within the ductal confines by a longitudinal incision into the superior ductal wall.

The following case report illustrates the technique proposed by the foregoing presentation.

CASE REPORT

A. L., a 30-year-old Negro man, was referred because of an acute left submaxillary sialadenitis and a secondarily associated left sublingual abscess (Figs. 4 and 5). An occlusal roentgenogram revealed the presence of two small salivary stones, each measuring about 4 mm. in diameter. The calcifications were approximately 6 mm. apart from one another and appeared to be situated at about the middle third of the duct (Fig. 6).

Fig. 6.—Preoperative occlusal radiograph revealing the presence of two diminutive calcifications in the oral floor (arrows).

Clinically, gross pus was evident in the left side of the floor of the mouth. This necessitated an intraoral incision and drainage and antibiotic therapy (penicillin). With the subsidence of the acute symptoms, surgical removal of the stones was planned.

As a preliminary to surgery, a deep suture was placed around Wharton's duct, anteriorly to the most forward stone. By soaking a silk suture in Ethiodol* (ethyl ester of iodinized fatty acids of poppyseed oil), radiopacity was obtained and accurate positioning could be confirmed by an occlusal x-ray view (Fig. 7). With the plica and the anterior suture as landmarks, a second ligature was then inserted around the duct approximately 2 cm. behind the initial one. This posterior suture was tightly tied, causing a constriction of the enclosed duct and adjacent soft tissues. As a consequence, application of tension to both sutures permitted the raising and immobilization of the operative site, in addition to the isolation of the sialoliths (Fig. 8).

When the preparatory steps were completed, an incision 1 cm. in length was made through the mucous membrane of the oral floor, commencing just behind the anterior suture,

*E. Fougera and Company, Hicksville, New York.

Fig. 7.—Preoperative occlusal view indicating placement of radiopaque anterior suture (arrows).

Fig. 8. Fig. 9.

Fig. 8.—Preoperative intraoral appearance following placement of localizing sutures (anterior and posterior).

Fig. 9.—Operative view with Wharton's duct exposed and drawn superiorly by means of a retracting suture.

and extended posteriorly. This incision was aligned lateral but parallel to the plica sublingualis.

By means of careful blunt dissection, the duct was visualized medial to the line of incision in a relatively superficial position. The duct was then segregated, and a retracting suture was placed around the structure (Fig. 9). By withdrawing the duct from the surrounding soft tissue, it was a relatively simple matter to extend the area of exposure almost

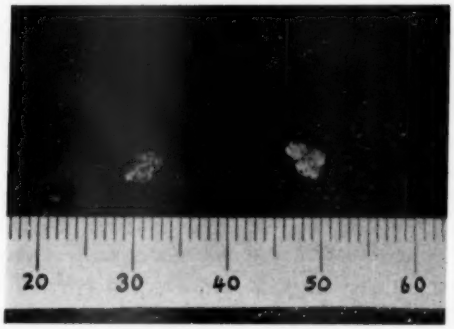

Fig. 10.—Two sialoliths recovered from Wharton's duct.

Fig. 11.—Postoperative true occlusal roentgenogram.

to the posterior suture. Upon completion of this surgical dissection, the two stones were located rapidly and removed (Fig. 10). A postoperative occlusal film confirmed the successful recovery of the calcific masses (Fig. 11).

COMMENTS

The key to success depends on the utilization of radiopaque localizing sutures. At the time of the actual surgery, no acceptable preformed radiopaque ligature was known to be available. A taut wire would have the disadvantage of cutting through soft tissues. Therefore, such a material was synthesized by soaking an ordinary silk suture in an iodinized oil for several days. Ethiodol was chosen since this contrast medium does not evoke a granulomatous reaction if retained within the tissues. Media containing poppyseed oil or peanut oil are contraindicated because of this unsatisfactory aspect. The one disadvantage noted in the immersion of a silk suture in contrast medium was the short-lived radiopaque quality of such a combination. Once inserted into the mouth, the bathing action of the saliva led to the rapid dilution and dissipation of the contrast solution and consequent diminution of its ability to block the passage of x-rays. This, in turn, necessitated a hurried x-ray technique and eliminated prolonged utilization of the diagnostic suture.

Subsequent communication with the Ethicon Suture Laboratories, Inc., New Brunswick, New Jersey, revealed the existence of an inert radiopaque suture made by braiding silk thread around a core of thin wire. This product undoubtedly should fulfill all the requirements without any of the aforementioned disadvantages.

SUMMARY

A simplified rational approach to the successful removal of small salivary stones is proposed and described. The basis of the procedure lies in the accurate localization and dissection of Wharton's duct.

REFERENCES

1. Shapiro, Harry: Applied Anatomy of the Head and Neck, ed. 2, Philadelphia, 1947, J. B. Lippincott Company, p. 179.
2. Shapiro, Harry: Applied Anatomy of the Head and Neck, ed. 1, Philadelphia, 1943, J. B. Lippincott Company, p. 167.

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DIAGNOSIS OF MANDIBULAR FRACTURES BY AUSCULTATION WITH PERCUSSION

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INTRODUCTION

THE presence of a fracture of the mandible can be determined by the auscultation-percussion test. With a little practice, the oral surgeon can master this simple procedure. This diagnostic technique is of added value in those cases in which roentgenographic examination must be delayed. It also gives added information to the radiologist for his study. This simple type of examination can be used in a negative way in those cases of trauma to the jaw in which the surgeon believes that a roentgenographic examination is not necessary.

METHOD

The bell of the stethoscope is placed firmly over the symphysis, and the patient is instructed to hold it. This leaves the right and left hands of the examiner free to percuss. Three taps are given alternately on the right and left sides. The examiner taps over the zygomatic arches first, then over the condyles, and finally over the angles. If there is loss of bone continuity between the area of percussion and the symphysis (area of auscultation), then the examiner will hear a dull note. This test should be done without the teeth in contact. In a tooth-contact position, the larger bone mass of the upper jaw and calvarium vibrate at a lower frequency. Variations in this procedure are evident. In a case involving fracture of the symphysis, the bell of the stethoscope can be placed alternately to the right and left of the midline while the examiner is percussing over the temporomandibular joint and angle areas.

COMMENT

Possibly the very simplicity of this diagnostic method is a deterrent to the student's becoming proficient. Attention should be given to the five factors involved in clinical success:

1. *The ear.* Any surgeon with normal hearing acuity can "educate" his ear to differentiate between the transmission of sound through uninterrupted bone and through a fractured bone. It has been my experience in teaching students that they do not listen long enough. They expect to complete the test in the same short time needed by the "educated" ear.

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2. *The stethoscope.* Either the bell or diaphragm type may be used. The former is designed for low-pitched heart murmurs and the latter for high-pitched ones. The ear plugs should be comfortable and should fit closely. A common mistake is to have plugs that are too small or to have a strong spring causing discomfort. The tubing should be as short as practical, with a thick wall and large bore.

3. *Background noise.* The room should be quiet enough to permit the surgeon to interpret correctly the sounds elicited.

4. *Percussion technique.* The strokes require automatic delivery, as the surgeon's entire attention is concentrated on listening. The pad of the middle finger is used as the plexor. The stroke should imitate a piano hammer. It should be of a perpendicular, quick-rebounding type. The quicker the percussing finger is withdrawn after striking, the clearer will be the note obtained. One should strike from the wrist, with the wrist completely relaxed. The pad of the middle finger is used. The percussing finger is bent at right angles. Uniformity of force is mandatory on the right and left sides.

5. *Auscultation technique.* The surgeon's whole attention should be concentrated on listening. The art depends not only upon the selective concentration of important sounds but also upon a knowledge of what extraneous sounds to disregard. The auscultator should be in a comfortable position. I prefer to close my eyes after the first series of percussion notes to avoid any visual distractions.

SUMMARY

The auscultation-percussion diagnostic test for fractures of the mandible is presented. The presence of a fracture of the mandible can be determined by its properties as a sound conductor. A stethoscope is placed firmly over the symphysis, and then the areas over the right and left zygomas, condyles, and angles are struck lightly with a finger. The sound of the blow is conducted downward through the bony substance of the mandible. Since transmission of sound through dense bone is more efficient than through less dense soft tissue, any break in the bony column will result in a decrease in the transmission of the sound.

Comment is made on the simplicity and value of this diagnostic aid. The factors involved in its execution are discussed.

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EXODONTIA

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HEADACHE AND THE SOURCE OF PAIN

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HEADACHES and facial pain often present a perplexing problem, not only to the patient but also to the physician. The latter should be aware that the teeth may be the source of pain, and in some this may be a factor. Wolff,[1] a noted neurologist, in his recent article contends that only a very small per cent have head pains because of defects in their teeth.

Early recognition of the presence of impacted teeth and proper surgical intervention will eliminate most of the complications for which impacted teeth are responsible. An example of this is presented in the following report of a case in which an impacted tooth caused persistent headaches.

Impacted teeth may cause vague and variable discomfort, sometimes completely symptomless. These teeth are often malformed and malpositioned, hidden completely or partially by bone and soft tissue. Thus, they may cause discomfort by pressure on the mandibular or maxillary nerves or on adjacent teeth, even rarely causing exposure of the pulp of the adjacent teeth. In some instances impacted teeth are associated with cysts. In the case of facial pains and headaches, routine x-ray studies of the jaws and teeth should be considered to rule out dental pathology. The technique for removal is determined by the size and location of the impacted teeth in that area.

CASE REPORT

Chief complaint: Patient J. E., a 19-year-old boy, was referred to the oral surgery clinic on Dec. 4, 1957, by his dentist for the removal of an impacted maxillary premolar.

History: The patient had been complaining of attacks of severe headaches for a period of two years. His attending physician could find no condition

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except the impacted tooth to which he could attribute the headaches. The physician insisted that this tooth be removed. The patient's history, personal and family, was noncontributory.

Fig. 1.

Fig. 2.

Figs. 1 and 2.—The occlusal and periapical dental roentgenograms demonstrate a horizontally impacted, unerupted premolar in the left palatine region. Note an area of rarefaction over the crown portion.

Oral examination: The checkup revealed a full complement of teeth, with the exception of the left upper first premolar which was missing. Although oral hygiene was adequate, the need for a prophylaxis was apparent. The teeth were in a good state of repair. A slight, firm bulging was noted in the left palatal premolar region.

General physical findings: General physical findings were normal.

Clinical impression: The impression was that of a horizontally impacted, unerupted maxillary premolar with a possible cystic lesion.

Laboratory findings: Laboratory examinations, including routine blood tests and urinalysis, were normal. There were no apparent tissue anomalies.

Roentgenographic examination: The occlusal and periapical dental roentgenograms demonstrated a horizontally impacted, unerupted premolar in the left palatine region. The tooth was completely imbedded in bone and lying between the molar roots. An area of rarefaction was visible over the crown portion and resembled a cystic lesion. Resorption was observed in the adjacent premolar root (Figs. 1 and 2).

Operative treatment: On Dec. 13, 1957, the patient was prepared for surgery. Preoperatively, 100 mg. of Seconal and 1/150 gr. of scopolamine were administered. After one hour, in the supine position, the patient was prepared and draped in the usual manner. A bilateral palatine block was given, following induction of local anesthesia with 1.5 per cent Primacaine.

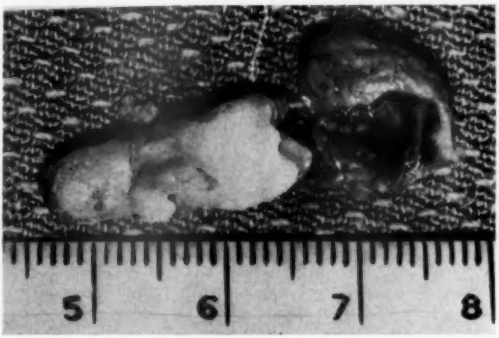

Fig. 3.—Gross specimen consists of a premolar and a detached follicle.

The incision was made with a #11 blade, freeing the attached gingivae from the left palatal aspect of the teeth. By blunt dissection, the mucoperiosteum was elevated and retracted from the left cuspid-second molar region. A gauze pack was placed in the mouth to prevent aspiration of blood. The palatal bone was visualized. The tooth was embedded under thick cortical bone, which was cut away with a sharp diamond cutting burr. The overlying bone was thus removed, and the tooth was visualized. Tissue resembling a cystic sac enveloped the crown and was enucleated in toto with the blunt end of a curette. The tooth was delivered with the help of a Potts elevator. The palatal root of the second premolar showed evidence of resorption. The wound was irrigated with warm saline solution. The palatal mucoperiosteum was approximated and, through the interdental spaces, sutured to the labial mucosa

with 00000 nylon suture material. A petrolatum gauze pack was placed as a pressure dressing to prevent a hematoma and postoperative swelling. The pack was retained with 0 braided black silk through the interdental spaces.

Postoperative treatment: Instructions for postoperative care included (1) clear liquids for two days, (2) sedation for pain, (3) ice bag over the face, (4) bed rest, and (5) oral rinses with warm saline. No antibiotics were prescribed. The patient was discharged to go home with his parents. The specimen was sent for histologic examination.

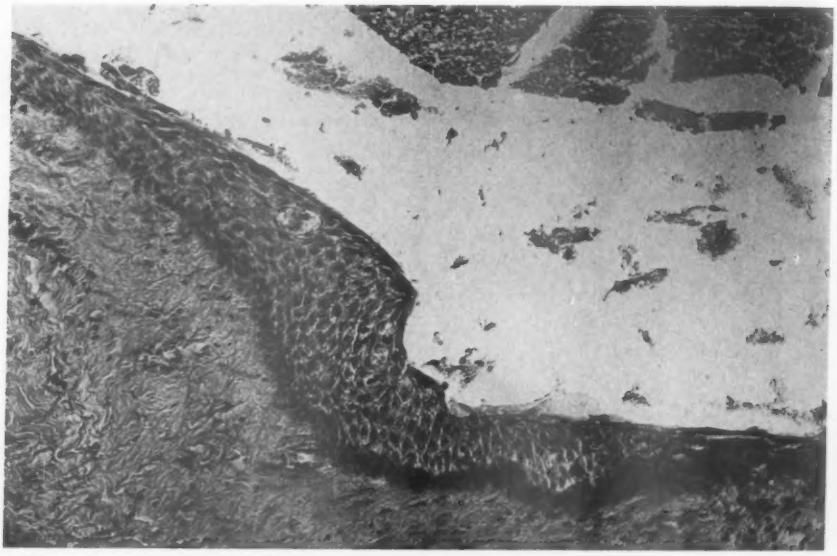

Fig. 4.—Photomicrograph showing "follicular cyst."

Postoperative course: The pack was removed on the third day. The wound was irrigated with warm saline and showed a normal healing. The remaining gingival sutures were removed on the tenth day. Recovery and healing were uncomplicated and uneventful. The wound healed completely in twenty days.

Pathologic report: The formalin-fixed specimen (Fig. 3) consisted of a premolar and a detached follicle which together measured 2.5 by 1.6 by 1.2 cm. A thin, hypoplastic defect encircled the crown of the tooth midway to the cervical line.

The microscopic examination of the specimen showed it to consist of a thick, collagenous, connective-tissue wall, rich in nuclei and showing occasional hemosiderin crystals. Toward the lumen were small aggregates of plasma cells and lymphocytes. The lumen was partially lined by remnants of a stratified squamous epithelium (Fig. 4). A few bone spicules were present.

Diagnosis: Follicular cyst, secondarily infected.

Follow-up: The six-month follow-up and postoperative radiographs (Figs. 5 and 6) showed normal findings and healing, and the patient was asymptomatic. The patient is free of headaches and is being seen periodically by his physician.

Fig. 5.

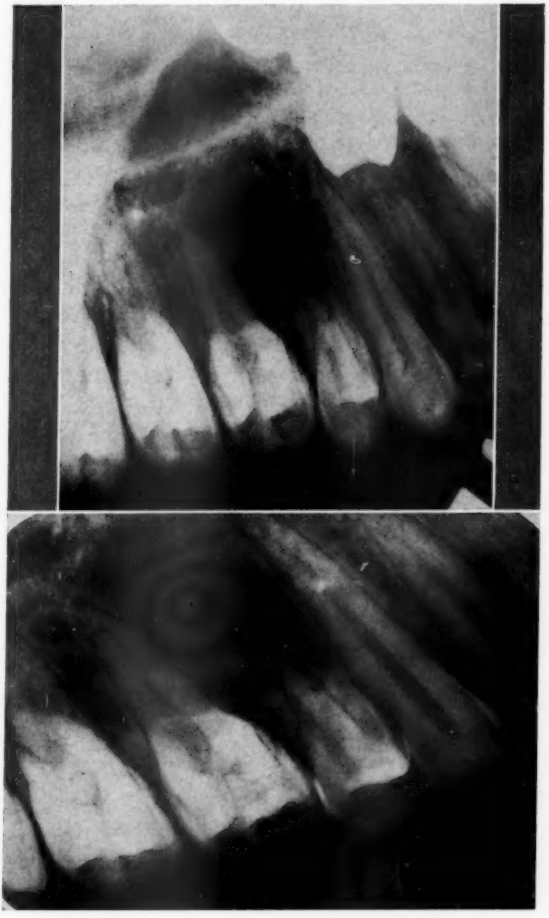

Fig. 6.

Figs. 5 and 6.—Postoperative roentgenograms show complete removal of impacted premolar and cyst and reveal normal healing.

REFERENCE

Wolff, H. G.: The Nature and Causation of Headache, J. D. Med. 14: 3-34, 1959.

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PERIODONTIA

RELATIONSHIP OF pH TO CALCULOUS PRECIPITATION

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Most physicians, if asked to name the most common disease afflicting mankind, would answer "upper respiratory infection," or the so-called common cold, and this is perhaps a valid conclusion in the adult. However, as pointed out by Robinson[24] and others, for the age period between 4 and 25 years the incidence of dental caries is double that of the common cold. This may be the chief reason that research in recent times has been concentrated so heavily on control of caries, with dangerous neglect of periodontitis or so-called pyorrhea, the primary reason for the loss of teeth in adults (of whom 80 per cent in this country are wearing dentures at the age of 65). Salivary calculus deposited on the teeth acts as an abrasive on the surrounding gingiva and initiates pocket formation as the epithelial attachment migrates down the root of the tooth. Debris settles in these pockets and forms an excellent culture medium for bacteria, some of which are pyogenic. The condition is manifested clinically by the purulent material that may be expressed from the gingival sulcus by lightly stroking the gingiva; in other words, pyorrhea develops, and this often necessitates removal of otherwise healthy teeth.

Years ago G. V. Black observed that persons with rampant caries were usually free of calculus, whereas for the most part those with heavy deposits of calculus and advanced pyorrhea did not have dental decay. This paradoxical situation has long been shrouded in mystery; at present, however, with more light cast on the etiology of caries and the initiation of calculous precipitation, the reasons for this relationship are more apparent, as are the dangers inherent in reversing one of the two processes.[26]

The phenomenon of decay is predicated in brief on the production of acid by lactobacilli that utilize carbohydrate as a substrate. The apatite crystal of enamel is calcium phosphochloride, which is soluble below pH 5.5; the lactobacilli can bring the pH down to 3, thus dissolving the enamel. Various methods and agents have been proposed to evaluate this chain of events.[1-3, 5-9, 15-19]

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At Ohio State University attempts were made to eliminate the carbohydrate substrate by diet. This carbohydrate-free diet, if maintained for two weeks, will alter the oral flora and protect against decay for as long as six months; however, it represents an impractical method at present. Robinson, Goldman and others[24] advocate brushing the teeth immediately after carbohydrate has been eaten; to date, this is perhaps the most reliable method for control of caries. The use of fluorides in drinking water and toothpastes is an attempt to strengthen the enamel by a transhalogenation reaction which results in an acid-resistant apatite molecule in which chloride is replaced by fluoride. In many respects, this approach to the problem is ideal.[20] The University of Chicago group, under Gottlieb, introduced dibasic ammoniated toothpastes in an attempt to neutralize the bacterial products and obviate acid dissolution of teeth. Many toothpastes, mouthwashes, chewing gums, and so forth at present have ammoniated compounds incorporated in them, often in combination with anti-enzymes (such as sodium lauryl sarcosinate) to prevent utilization of carbohydrate in anaerobic glycogenolysis, and for them is claimed the ability to maintain the pH at high levels (8 to 9) for prolonged periods (in excess of twenty-four hours with a single application or intermittent use).[10, 21] Herein lies a danger, since elevation of the pH in the mouth makes conditions ideal for precipitation of calculus and the beginnings of pyorrhea.

Not all the factors involved in the precipitation of calculus are known as yet.[13, 14, 22, 27, 31] The exact composition of calculus is complex, as Hawk and co-workers[12] have shown; however, basically 70 per cent of it is calcium phosphate, with carbonates constituting most of the remainder.[11] Investigators such as Waerhaug[28] have expressed the view that calculus is deposited subgingivally directly from the blood stream. However, Wah Leung[29, 30] and Morgan[31] showed that ten extracted teeth dipped into activated saliva (saliva obtained by chewing paraffin and expectorating) were coated with 17 mg. of calculus in two weeks. They further showed the effect that drying of the teeth has in formation of calculus. The role of salivary colloids in maintaining crystalloids in solution is discussed by Dewar and Parfitt[4] and others.[14, 23] Rapp,[23] in proving the presence of salivary carbonic anhydrase, postulated rapid changes in pH at the gingival margin owing to this enzyme and said that "a moderate amount of alkalinization of saliva with tendency to calculus formation could cause sufficient oversaturation of calcium and phosphate salts in the saliva to facilitate precipitation. . . ." In these investigations the common denominator is seemingly a pH change toward the more basic values.

One then wonders what effects, if any, alteration of the pH of 6.8 in normal saliva[25] by highly basic toothpastes and mouthwashes will produce, and whether there is danger, at least in adults, that a possibly overzealous attack on acid-causing decay may, in reality, represent trading decay for calculus and the much more serious implications of pyorrhea in the adult. It is therefore logical to establish the exact nature of the relationship between pH and the precipitation of calculus.

PRESENT INVESTIGATION

Samples of calculus were obtained by scaling the teeth of unselected dental outpatients. Each specimen was dissolved in 10 ml. of concentrated hydrochloric acid, and aliquots of 2 ml. were placed in 25 ml. flasks. Each aliquot was titrated with 10 per cent solution of sodium hydroxide to end points ranging from a pH of 4 through a pH of 11.5. The precipitate was filtered on ashless filter paper, dried in an oven for thirty minutes at 115° C., placed in a desiccator for twenty-four hours, and weighed, the weight of the filter paper being subtracted. The Beckman meter was used in determining pH. The data obtained are presented in Table I and in Fig. 1.

TABLE I. PERCENTAGE OF CALCULUS PRECIPITATED AT DIFFERENT pH VALUES

GROUP I (LOW pH VALUES)		GROUP II (MIDDLE pH VALUES)		GROUP III (HIGH pH VALUES)	
pH	CALCULUS PRECIPITATED (PER CENT)	pH	CALCULUS PRECIPITATED (PER CENT)	pH	CALCULUS PRECIPITATED (PER CENT)
4.4	18.0	6.55	22.2	8.40	26.0
4.6	20.5	6.55	24.0	8.75	30.5
4.7	18.7	6.55	27.0	8.85	28.1
4.7	19.0	6.60	23.7	8.90	25.9
4.9	19.7	6.60	29.5	8.90	24.7
5.2	19.0	6.70	26.0	9.00	26.0
5.3	20.6	6.70	27.5	9.05	29.3
5.45	24.3	6.80	19.5	9.10	25.6
5.50	22.2	7.00	29.4	9.30	24.1
5.8	22.8	7.05	25.0	9.55	29.5
5.9	23.5	7.05	23.0	9.90	29.0
6.05	19.0	7.45	27.0	10.25	27.0
6.05	24.0	7.90	30.7	10.60	28.1
6.05	24.7	8.15	25.5	11.50	25.4
		8.30	27.0	11.70	25.3
		8.35	26.3		
$Mean_I = 21.1$		$Mean_{II} = 25.8$		$Mean_{III} = 27.0$	
$n = 14$		$n = 16$		$n = 15$	
$\Sigma x = 296.0$		$\Sigma x = 413.3$		$\Sigma x = 404.5$	
$\Sigma x^2 = 6330.9$		$\Sigma x^2 = 10{,}803.07$		$\Sigma x^2 = 10{,}962.53$	
$S.D._{I,II} = 2.518$	$t = 1.26$	$P = 0.2\text{-}0.3$			
$S.D._{I,III} = 2.17$	$t = 7.27$	$P = <.001$			
$S.D._{I,II+III} = 2.431$	$t = 6.64$	$P = <.001$		$Mean_{II+III} = 26.4$	

Since the results of this experiment were obtained in vitro, one must be cautious in the clinical interpolation of them. The data suggest, however, that whereas elevation of the oral pH increases the risk of producing instability of the constituents of salivary calculus, this risk is not increased significantly in the change from the nearly neutral pH of saliva to the much more basic pH of the various dental products. The use of products of increased acidity (pH of less than 5.5), though significantly safer from the standpoint of calculous precipitation and therefore production of pyorrhea, is nonetheless impractical because of the danger of decalcification of the apatite crystal of enamel.

It is concluded that (1) the amount of calculus precipitated increases as the pH increases, (2) the difference between the amount of calculus precipitated

at the pH of saliva (6.8) and the amount precipitated at the upper limit of prolonged tolerance by the oral mucosa (8.5) is not statistically significant, and (3) there is a 24 per cent increase in the amount of calculus precipitated in the pH range of 6.5 to 8.5 as compared to the amount precipitated in the range of 4.5 to 6.

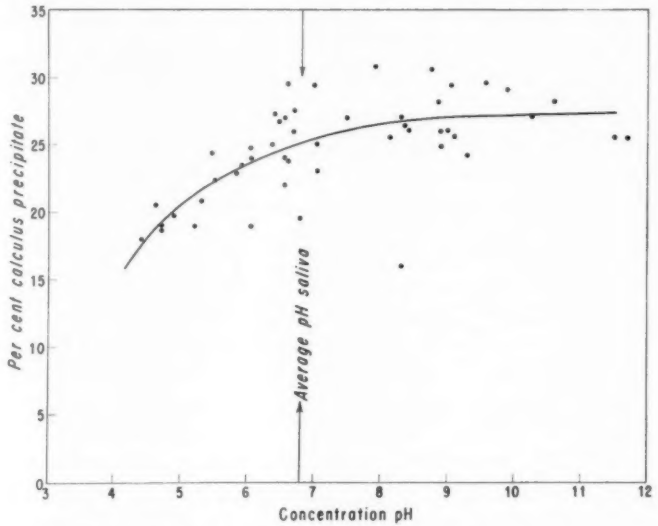

Fig. 1.—Relationship of calculous precipitation to pH. Each dot represents one observation.

REFERENCES

1. Bruckner, R. J., Hill, T. J., and Wollpert, B. J.: Measurement of Dental Caries Incidence in School Children Using a Sodium Bicarbonate Dentifrice, J. D. Res. **31**: 105-112, 1952.
2. Cohen, A., and Donzanti, A.: Two Year Clinical Study of Caries Control With High-Urea Ammoniated Dentifrice, J. A. Dent. A. **49**: 185-190, 1954.
3. Davies, G. N., and King, R. M.: The Effectiveness of an Ammonium Ion Toothpowder in the Control of Dental Caries, J. D. Res. **30**: 645-655, 1951.
4. Dewar, M. R., and Parfitt, G. J.: An Investigation of the Physical Properties of Saliva and Their Relationship to the Mucin Content, J. D. Res. **33**: 596-605, 1954.
5. Dirks, O. B., Winkler, K. C., and Van Aken, J.: A Reproducible Method for Caries Evaluation. III. Test in a Therapeutic Experiment With an Ammoniated Dentifrice, J. D. Res. **32**: 18-26, 1953.
6. Ennever, J., Robinson, H. B. G., and Kitchin, P. C.: Effect of Three Diphenylmethane Derivatives on Acid Production in Saliva and on Logarithmic Growth of Oral Lactobacillus, J. D. Res. **32**: 61-64, 1953.
7. Forscher, B. K., and Hess, W. C.: The Validity of Plaque pH Measurements as a Method of Evaluating Therapeutic Agents, J. Am. Dent. A. **48**: 134-139, 1954.
8. Forscher, B. K., Paulsen, A. G., and Hess, W. C.: The pH of the Periodontal Pocket and the Glycogen Content of the Adjacent Tissue, J. D. Res. **33**: 444-453, 1954.
9. Fosdick, L. S.: Enzyme Inhibitory Agents, J. Am. Dent. A. **48**: 19-21, 1954.
10. Fosdick, L. S., Calandra, J. C., Blackwell, R. Q., and Burrill, J. H.: A New Approach to the Problem of Dental Caries Control, J. D. Res. **32**: 486-496, 1953.
11. Grossman, L. I.: Effect of Chemical Agents on a Calculus Substitute, ORAL SURG., ORAL MED. & ORAL PATH. **7**: 484-487, 1954.
12. Hawk, P. B., Oser, B. L., and Summerson, W. H.: Practical Physiological Chemistry, ed. 13, New York, 1954, The Blakiston Company.

13. Helman, E. Z., and Mitchell, D. F.: Phosphatase in Human Saliva: Its Relationship to Calculus and Lactobacillus Counts, J. D. Res. **33**: 335-338, 1954.
14. Jensen, A. T., and Dan, Marianne: Crystallography of Dental Calculus and the Precipitation of Certain Calcium Phosphates, J. D. Res. **33**: 741-750, 1954.
15. Kessel, R. G., O'Donnell, J. F., and Wallace, D. A.: Effects of Single Brushings With Combinations of Dibasic Ammonium Phosphate and Urea on Human Salivary Lactobacillus Counts, J. Am. Dent. A. **48**: 8-13, 1954.
16. Kniesner, A. H.: Efficacy of Medicated Dentifrices in the Practice of Dentistry, J. Am. Dent. A. **48**: 22-25, 1954.
17. Kutscher, A. H., and Chilton, N. W.: Observations on Clinical Use of Chlorophyll Dentifrice, J. Am. Dent. A. **46**: 420-422, 1953.
18. Lefkowitz, William, and Venti, V. I.: A Preliminary Clinical Report on Caries Control With a High Urea Ammoniated Dentifrice, ORAL SURG., ORAL MED. & ORAL PATH. **4**: 1576-1580, 1951.
19. Malone, A. J.: The Effect of a Therapeutic Dentifrice on the Dental Needs of Children (Abst. 105), J. D. Res. **34**: 710, 1955.
20. Muhler, J. C., Radike, A. W., Nebergall, W. H., and Day, H. G.: The Effect of a Stannous Fluoride-Containing Dentifrice on Dental Caries in Adults, J. D. Res. **35**: 49-53, 1956.
21. Nolte, W. A., and Sumter, S. A.: In Vitro Changes in pH of Dental Plaque Material and Surrounding Saliva, J. D. Res. **35**: 83-89, 1956.
22. Rapp, G. W.: The Biochemistry of Oral Calculus. I. Conditions Predisposing to Oral Calculus Deposition, J. Am. Dent. A. **32**: 1368-1372, 1945.
23. Rapp, G. W.: The Biochemistry of Oral Calculus. II. The Presence of Carbonic Anhydrase in Human Saliva, J. Am. Dent. A. **33**: 191-194, 1946.
24. Robinson, H. B. G.: Personal communication to the authors.
25. Turner, N. C., and Meyer, J. Y.: Comparative Results of Tests on Parotid Saliva, on Mixed Saliva, and on Mixed Saliva Without Parotid Saliva, Cahiers Odonto-Stomatologiques **2**: 19-32, 1952.
26. Turner, N. C., Scribner, J. H., and Bell, J. T.: The Relationship of Titratable Acidity to Titratable Alkalinity and pH to the Incidence of Dental Caries, J. D. Res. **33**: 55-61, 1954.
27. Van Huysen, G., and Bhatavadaker, V.: The Inhibition of Calculus Formed In Vitro (Abst. 162), J. D. Res. **34**: 733, 1955.
28. Waerhaug, Jens: Source of Mineral Salts in Subgingival Calculus, J. D. Res. **34**: 563-568, 1955.
29. Wah Leung, S.: A New Method for the In Vitro Production of Artificial Calculus (Abst. 138), J. D. Res. **32**: 689, 1953.
30. Wah Leung, S.: Further Studies on the Effect of Lactones on Synthetic Calculus Formation (Abst. 95), J. D. Res. **34**: 706, 1955.
31. Wah Leung, S., and Morgan, P. V.: Calculus Formation From Saliva as Influenced by an Altered Bacterial Flora (Abst. 139), J. D. Res. **32**: 690, 1953.

ORAL MEDICINE

PRIMARY HERPES SIMPLEX VIRUS INFECTION IN AN ADULT

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ALTHOUGH approximately 90 per cent of the population over 15 years of age has specific antibodies against the herpes simplex virus, recognizable primary infection occurs in less than 1 per cent of the population.[1] When seen, the disease is usually in children from 2 to 5 years of age, giving rise to such well-known manifestations as acute herpetic gingivostomatitis or vulvovaginitis and occasionally to inoculation herpes simplex resulting from direct inoculation of the virus into an abrasion or laceration.[2-4] The latter is attended by discrete vesicles grouped in a characteristic manner at the inoculation site, accompanied by enlargement of the regional lymph nodes and often by fever and systemic manifestations. Symptoms appear after an incubation period of approximately five days (sometimes two or three days) and last approximately 10 to 14 days. Initial infection is also followed by the appearance in five to ten days of specific antibodies which persist for many years. Recurrent herpes simplex may occur at the same site months or years later.

A survey was made of the literature for reports of primary herpetic infection in adults. Few were found in which the diagnosis of a primary rather than a recurrent infection could be made with any degree of certainty. We found only one case of a generalized infection with severe constitutional symptoms in which the diagnosis was adequately supported by laboratory evidence.[5] In two cases a presumptive diagnosis of inoculation herpes simplex of the skin following clinical exposure to the virus was warranted on the basis of the course and symptoms.[6, 7]

The object of this report is to direct attention to a case of primary clinical herpes virus infection in a dental student who attended a patient with recurrent herpes simplex of the mouth and to define the criteria for the diagnosis of a primary infection. To our knowledge, this is the first recorded example of this manner of transmission of the virus.

From the Department of Microbiology, New York University, College of Dentistry, and from the Department of Dermatology and Syphilology, New York University, Postgraduate Medical School and the Skin and Cancer Unit, University Hospital.

CASE REPORT

History.—A 24-year-old white male dental student, in the course of his training at the dental college, performed dental procedures on March 11, 12, 18, and 20 on a patient with "multiple fever blisters." The patient was a 35-year-old white woman who gave a history of recurrent herpes labialis. On March 17 the student noticed a single raised lesion on the palmar surface of his left index finger; the lesion ruptured with drainage of a clear fluid. Within the next four or five days a number of vesicles appeared in close proximity to the initial lesion. Some of the vesicles became confluent, forming a tender, round, firm red plaque approximately 1.5 cm. in diameter projecting 1 to 2 mm. above the involved site.

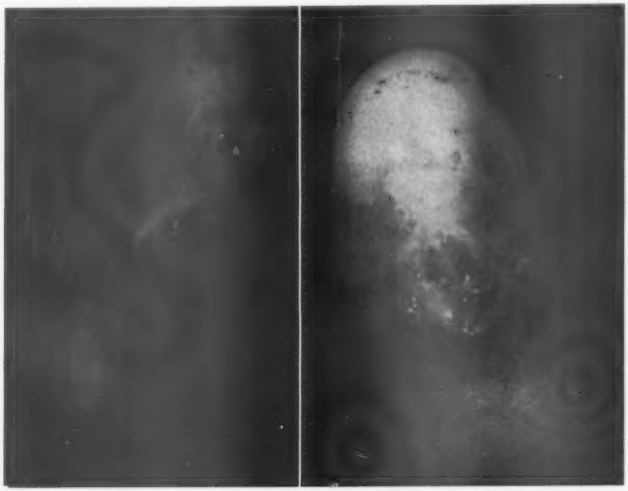

Fig. 1.—Crusted herpetic lesion on palmar surface of left index finger.

Fig. 2.—Single vesicular papule on lateral surface of terminal phalanx of right index finger.

On March 25 the student felt ill and feverish and noted that the left axillary lymph nodes were somewhat enlarged and tender. The patient could not recall having had any signs or symptoms of infection with herpes simplex.

Physical Examination.—The patient reported for examination at the Skin and Cancer Unit on March 26, 1957. A herpetic plaque, measuring approximately 2 by 3 cm., was found on the palmar surface of the left second finger (Fig. 1). The axillary lymph nodes were moderately enlarged and slightly tender. The patient looked ill, and his temperature was 101° F. On March 28 a small vesicopapule was observed on the palmar surface of the terminal phalanx of the right index finger (Fig. 2).

Laboratory Findings.—Fluid was aspirated from the lesions of both fingers and suspended in a small amount of sterile saline. The mixed saline suspensions were then inoculated into the scarified cornea of a rabbit and intracranially into three mice.

Rabbit: The scarified cornea showed a keratoconjunctivitis in eighteen hours. A purulent exudate and several small vesicles developed along the course of the scratches. The nictitating membrane was red and swollen.

Fig. 3.—Isolated plaques on the chorioallantoic membrane of a chick embryo.

Mice: Two of the three mice developed a herpetic encephalitis; one died within twenty-four hours and another within thirty-six hours. Petechial hemorrhage and discoloration were found in the cortical tissue. Smears of homogenized tissue revealed the presence of type A inclusion bodies. Homogenates of the mouse brains were then forwarded for confirmation to the Virus Laboratory, Diagnostic Division, Bureau of Laboratories, New York City Department of health.

Embryonated chick eggs: Several passages were needed before characteristic lesions were noted. Many small raised white plaques were seen on the harvested chorioallantoic membrane (Fig. 3). Stained preparations revealed the presence of intranuclear type A inclusion bodies in many of the proliferating cells.

*Serology:** The virus was identified as herpes simplex by neutralization tests. Complement fixation studies utilizing the herpes simplex virus isolate as the antigen gave the following results: blood specimen drawn April 1, 1957—positive 1:16 dilution; April 11, 1957—positive 1:32 dilution; June 6, 1957—positive 1:32 dilution.

COMMENT

A clinical diagnosis of primary herpes simplex infection of the index fingers was based on the negative history for previous episodes, the history of exposure to a typical case of recurrent herpes labialis, the distribution of the lesions on the fingers which were in contact with the infected mucous membranes in the course of retracting the patient's lips and cheeks, and the associated fever, malaise, and lymphadenopathy. One may assume that there was ample opportunity for direct inoculation of the virus in the course of carrying out the dental procedures. The eruption on the left index finger appeared five days after the initial exposure and that on the right index finger appeared a week after the last exposure. The interval may be explained by the order in which the contact was made.

The virus in question was identified by standard laboratory procedures as herpes simplex. A twofold increase in the titer of complement-fixing antibodies was also demonstrated. Presumably, this increase might have been greater if the first blood specimen had been drawn earlier in the course of the illness.

We are in agreement with Kilbourne and Horsfall[8] that the absence of demonstrable specific antibodies during the acute phase and the demonstration of specific antibodies during convalescence are essential to the diagnosis of primary herpetic infection. It is felt that the twofold increase in the titer of complement-fixing antibodies in this case is significant. The latter finding, as well as the history and clinical findings, was interpreted as supportive evidence of a primary rather than a recurrent clinical infection.

The criteria for a definitive diagnosis of primary herpetic infection may be summarized as follows: (1) a negative history for earlier episodes, (2) a history of exposure to herpes simplex virus, (3) an incubation period of approximately five days, (4) the development of characteristic lesions from which the virus can be isolated, (5) regional lymphadenopathy with greater or lesser systemic manifestations (for example, fever), and (6) finally and most important the demonstration of a sizable increase in the specific antibody titer.

The vulnerability of the dentist in the dentist-patient relationship assumes importance in view of the development of a herpetic infection in a

*We are indebted to Dr. Daniel Widelock and Miss Olga Simonovic of the Virus Laboratory, Diagnostic Division of the Bureau of Laboratories, Department of Health, The City of New York, for this report.

susceptible person in contact with the disease in a patient. This case should serve to emphasize the need for caution on the part of the dental practitioner in the management of patients with manifest herpetic lesions.

SUMMARY

A case of primary inoculation of a dental student's fingers with herpes simplex virus has been reported. The infection in this case resulted from exposure to a patient with recurrent herpes labialis. The need for recognizing this hazard in dental practice has been discussed and the criteria for the diagnosis have been defined.

REFERENCES

1. Blank, H., and Rake, G.: Viral and Rickettsial Diseases of the Skin, Eye and Mucous Membranes of Man, ed. 1, Boston, 1955, Little, Brown & Company.
2. Findlay, G. M., and MacCallum, F. O.: Recurrent Traumatic Herpes, Lancet **1**: 259, 1940.
3. Scheer, K.: Direkte Uebertragung des Herpes Simplex von Mensch zu Mensch, München. med. Wchnschr. **78**: 613, 1931.
4. Brain, R. T.: The Clinical Vagaries of the Herpes Virus, Brit. M. J. **1**: 1061, 1956.
5. Kipping, R. H., and Downie, A. W.: Generalized Infection With the Virus of Herpes Simplex, Brit. M. J. **1**: 247, 1948.
6. Hruszek, H.: Beitrag zum Problem der natürlichen Übertragung des Herpes virus von Mensch zu Mensch; Die venerische Ansteckung, Dermat. Wchnschr. **105**: 1150, 1937.
7. Simpson, J. R.: Kaposi Varicelliform Eruption—Direct Transmission to a Nurse, Brit. J. Dermat. **65**: 139, 1953.
8. Kilbourne, E. D., and Horsfall, F. L., Jr.: Primary Herpes Simplex Virus Infection of the Adult, A. M. A. Arch. Int. Med. **88**: 495, 1951.

ORAL ANATOMY AND PHYSIOLOGY

AN INVESTIGATION OF THE MECHANISM OF NEURAL IMPULSE TRANSMISSION IN HUMAN TEETH

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INTRODUCTION

THE mechanism of pain transmission through dentine is a subject of significant clinical interest. Consequently, it has been the object of much investigation. Although considerable evidence has been presented concerning the nervous system within the dental pulp, there is still a lack of definitive information concerning the physiologic mechanism by which neural impulses pass through dentine. It is the purpose of this study to determine whether chemical substances associated with neural impulse conduction are present within human teeth.

Acetylcholinesterase and acetylcholine are believed to play an essential role in the transmission of neural impulses.[1] Elliott,[2] in 1905, first suggested a chemical mediation of neural impulses, and since the discovery of the chemical substance by Loewi[3] and its later identification as acetylcholine by Dale and Feldberg,[4] the chemical theory of impulse transmission has received much attention. It is believed that associated with neural impulse transmission are the liberation of acetylcholine along a nerve and the subsequent hydrolysis of acetylcholine by the enzyme acetylcholinesterase (AChE), thus terminating neural activity.[5] The presence of AChE is therefore believed to be indicative of the existence of acetylcholine and thus of the cholingeric mechanism.[6]

Cholinesterase was demonstrated first by Plattner[7] and later by Engelhart and Loewi.[8] Further research disclosed the presence of two or more cholinesterases, a specific and a nonspecific type.[9] The specific cholinesterase was

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found primarily in the brain, along nerves, at synapses, at motor endplates,[10-13] and in red blood cells.[14] The nonspecific cholinesterase was found in blood serum[15, 16] and in liver.[17, 18] The specific and the nonspecific cholinesterases are differentiated by their selectivity of action on a variety of substrates. Specific cholinesterase does not hydrolyze butyrylthiocholine but does hydrolyze acetylthiocholine. Nonspecific cholinesterase will hydrolyze both the butyrylthiocholine and the acetylthiocholine substrates.[19] An inhibitor, di-isopropyl fluorophosphate* (DFP), at a concentration of 10^{-6} M has been found to completely inactivate nonspecific cholinesterase.[17]

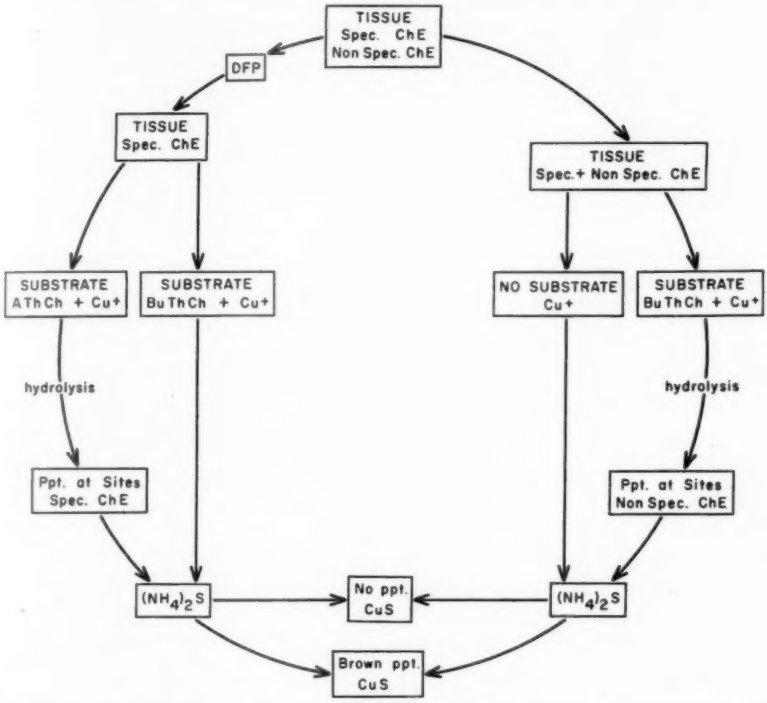

Fig. 1.—Diagram of techniques involved in the localization of the sites of activity of specific and nonspecific acetylcholinesterase.

On the basis of substrate hydrolysis, Koelle and Friedenwald[20] demonstrated a histochemical method for identifying sites of cholinesterase activity. The principle of the technique is as follows: tissues containing the specific enzyme are incubated in the presence of acetylthiocholine and copper ions, and the resulting precipitate of copper thiocholine appears at the sites of enzymatic activity. This precipitate is subsequently treated with ammonium sulfide to produce a more visible brownish copper sulfide precipitate at the sites of specific cholinesterase activity.

*Di-isopropyl fluorophosphate was generously supplied by Dr. William H. Summerson of the U. S. Army Chemical Warfare Laboratories, Army Chemical Center, Maryland.

It is, therefore, the purpose of this investigation to determine the presence or absence of a specific cholinesterase system in the pulp and dentine of human teeth and, if such a system is present, to compare its location with the known location of nerves.

MATERIALS AND METHODS

The methods of Koelle and Friedenwald[20] and the subsequent modifications of Pearse,[21] Churchill and associates,[22] and Avery and Rapp[23] were utilized in the study of both specific and nonspecific esterases in human teeth.

Forty freshly extracted human teeth of the permanent dentition were collected and immediately prepared. On a calcified-tissue-slicing machine the teeth were cut sufficiently thin (50 micra) for microscopic study. These tissues were then divided into four experimental groups. The first group was treated with 10^{-6} M di-isopropyl fluorophosphate (DFP) for thirty minutes at 37° C. and then incubated with acetylthiocholine (AThCh) for sixteen hours to reveal the sites of activity of the specific cholinesterase. The second group of tissues was incubated in a substrate of butyrylthiocholine (BuThCh) for twelve hours at 37° C. to indicate the sites of the nonspecific cholinesterase. The third group of tissues served as a control and was incubated without a substrate. The fourth group of tissues also acted as a control, being treated with DFP and then incubated with BuThCh.

All the teeth then were treated with ammonium sulfide, and the resulting precipitate of copper sulfide indicated the sites of cholinesterase activity. The calcified tooth sections then were fixed, dehydrated, and mounted. By these methods the location of both specific and nonspecific cholinesterase activity was revealed in human teeth.

RESULTS

Specific cholinesterase was observed to be present in generally consistent locations and concentrations in all of the forty permanent teeth studied. In the pulp the areas of greatest concentration appeared to be in the nerve trunks and in a narrow band bordering the predentine of the coronal pulp chamber (Fig. 2). The width of the band included the row of odontoblastic cells and the adjacent cell-free zone and appeared most intense in the parietal layer of nerve fibers. The band underlies the dentine of the entire crown of the tooth (Figs. 2 and 4). In some teeth of older age groups the band extends apically along the dentine of the root canals. Examination of the dentine revealed that Tomes' fibers, the protoplasmic extensions of the odontoblasts, were specific cholinesterase positive (Figs. 6, 7, and 8). An increased intensity of specific cholinesterase was apparent at the dentino-enamel junction, probably because of the branching of Tomes' fibers (Fig. 8). Specific cholinesterase also appeared in the extensions of these fibers in the enamel. Upon examination of Tomes' fibers under higher magnification, secondary processes of these fibers appeared along most of their lengths and these processes were also cholinesterase

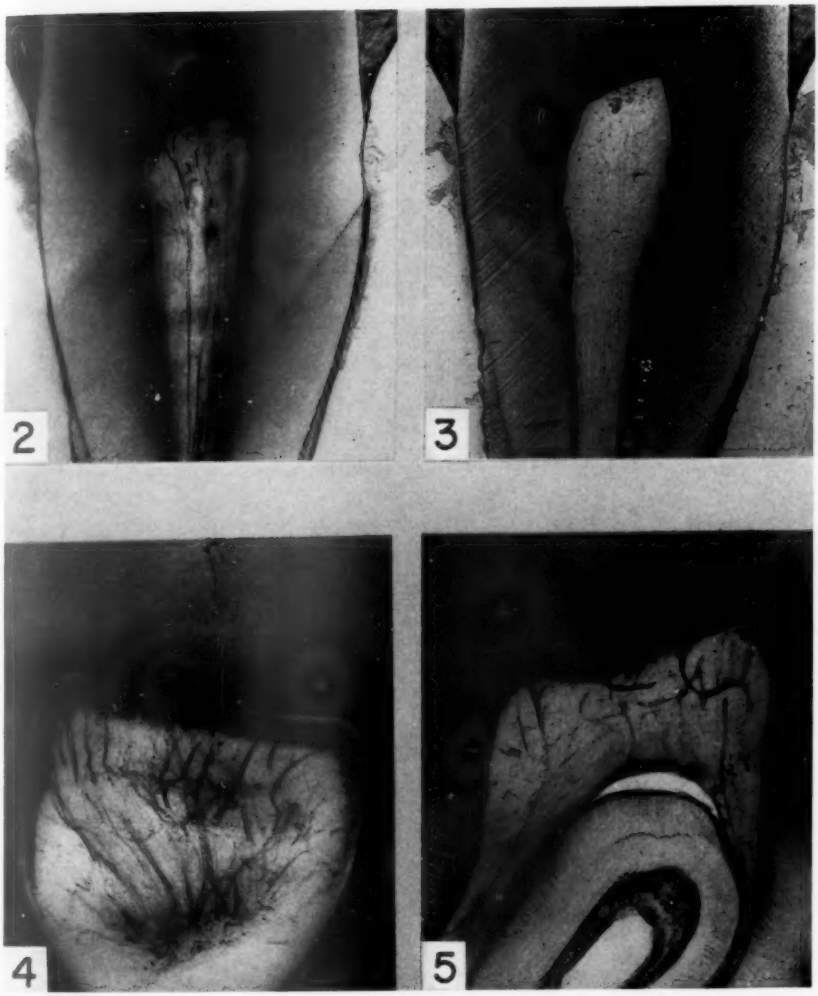

Fig. 2.—Tooth section treated with 10^{-6} M di-isopropyl fluorophosphate and acetylthiocholine to reveal the sites of specific cholinesterase. In the pulp an intense concentration of copper sulfide representing acetylcholinesterase is observed underlying the dentine of the coronal pulp chamber.

Fig. 3.—A control tooth section revealing the absence of reaction when DFP-treated tissue was incubated with butyrylthiocholine.

Fig. 4.—Pulp of human tooth revealing sites of activity of specific cholinesterase bordering the dentine which underlies the enamel of the crown.

Fig. 5.—Tooth section incubated with butyrylthiocholine to reveal the sites of activity of the nonspecific cholinesterase. The coronal blood vessels and the area adjacent to the predentine indicate activity as well as a diffuse reaction throughout the pulp.

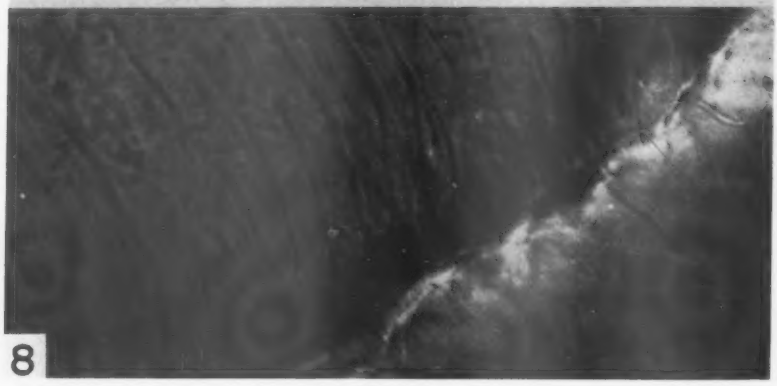

Fig. 6.—Area of dentine just peripheral to the predentine area revealing the intense concentration of specific cholinesterase in Tomes' fibers and their secondary processes. Although the minute processes were seen throughout the field, it was found possible to bring only a small area of them into focus at one time.

Fig. 7.—Area of dentine midway to dentino-enamel junction revealing presence of specific cholinesterase in Tomes' fibers and their secondary processes.

Fig. 8.—Dentino-enamel junction revealing presence of specific acetylcholinesterase in branching terminal parts of Tomes' fibers. The enzyme is present throughout each fiber but, because the upper left of this photograph is out of focus, the reaction is visible only at the dentino-enamel junction.

positive (Figs. 6 and 7). These minute fibrils appeared either to join adjacent Tomes' fibers or to terminate between fibers. It was noted that the predentine of this series of teeth was darkened by the copper sulfide precipitate.

With butyrylthiocholine serving as the substrate, concentrations of nonspecific cholinesterase were observed in the larger pulpal blood vessels as well as in the smaller ones near the odontoblasts. A zone of nonspecific cholinesterase activity was also seen underlying the predentine of the coronal pulp chamber (Fig. 5). The staining of this zone was less intense than that of the specific esterase and was diffused into the ground substance of the pulp. Tomes' fibers appeared stained, but to only a slight degree in comparison with the intense concentration of the specific cholinesterase. The predentine zone was again noted to be stained.

Upon examination of both control groups, no staining was seen throughout the pulp or in Tomes' fibers (Fig. 3). There was, however, staining of the predentine to an extent similar to that seen in the previous groups.

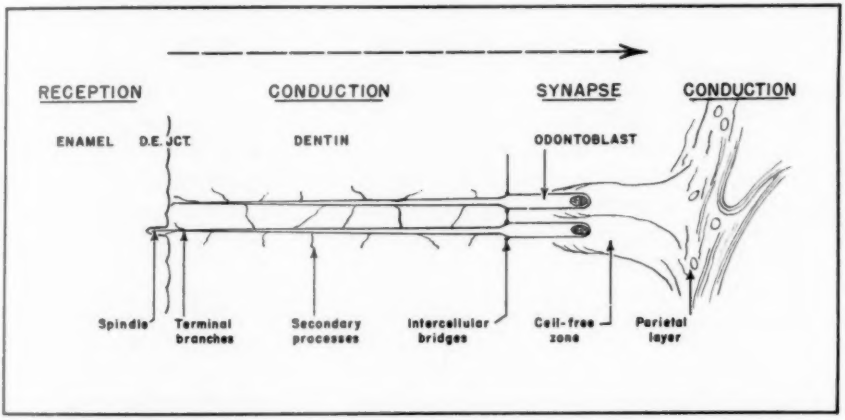

Fig. 9.—Diagram representing a possible mechanism of reception of pain at the dentinoenamel junction and transmission of pain to the odontoblast where a synapse occurs with the adjacent free nerve endings of the pulp. By means of the secondary processes of Tomes' fiber and the intercellular bridges of the odontoblasts, stimulation of a single Tomes' fiber could result in stimulation of all odontoblasts and free nerve endings of the coronal pulp.

DISCUSSION

The presence of specific cholinesterase in Tomes' fibers, from their terminal branches at the dentino-enamel junction to the odontoblasts, indicates a possible path of pain transmission through dentine. Furthermore, a synapse is indicated in the odontoblastic zone by the intense concentration of specific cholinesterase in this area. These findings are in agreement with clinical evidence of pain experience and also with the findings of numerous investigators, the most recent of whom (Bernick[24] and Rapp and associates[25]) reported no nerve fibers penetrating to any extent into the dentine, the majority terminating among the odontoblasts. It is believed that the presence of specific cholinesterase in the

odontoblast and its extension does not necessarily mean that they are neural elements. As Brashear[26] aptly explained, the odontoblast may well function in a neural capacity, although it may not necessarily be a neural cell. He referred to examples of free nerve endings in the skin of the corium of the palm or the cornea of the eye which are stimulated by means of non-neural elements.

Modification of the techniques of Koelle and Friedenwald[20] and of Koelle[17, 27, 28] for the study of calcified tissues presented certain problems in technical management of the tissues and interpretation of findings. In an effort to control false localizations of the sites of enzymatic activity, several procedures were instituted. Sectioning of all calcified tissue was done quickly and under a water spray to prevent temperature increases. In order to prevent enzymatic diffusion, the storage and incubation solutions contained high concentrations of sodium sulfate and the incubation solutions were also saturated with copper thiocholine. Whereas the chemicals necessary for the reaction penetrated the pulpal tissue readily, they did not diffuse through calcified dentine at the same rate. It was necessary, therefore, to cut the tooth samples in thicknesses of approximately 50 micra or less to permit diffusion of the reagents through the dentine. It was also necessary in these experiments to increase the incubation time to fourteen and sixteen hours for nonspecific and specific cholinesterase, respectively, to obtain significant precipitation for observation and photography. This probably is due partially to the dense character of the calcified tissue and the lower concentrations of the specific cholinesterase in sensory nerves as compared to cholinergic nerves. In this length of time some hydrolysis of acetylthiocholine and butyrylthiocholine probably occurs. What effects this may have on the reaction have not as yet been determined. In this respect, however, tissues of group 4, which were incubated in BuThCh for the same length of time, did not reveal any hydrolysis of the ester. Less mineralized areas, such as the predentine and carious dentine, were noted to contain needle-shaped crystals of copper thiocholine in the open meshwork of fibers. These crystals did not wash out in subsequent controlled washings. Thus, some degree of false localization was obtained. Since this staining was consistent even in the control tissues, these areas were regarded as artifacts. The significant deposition of specific cholinesterase in Tomes' fibers and pulpal nerve fibers as described was not seen in control groups and thus is believed to be a valid finding.

CONCLUSIONS

1. Specific cholinesterase is present in significant concentrations in nerves of the pulp, in a localized band in the pulp underlying the predentine of the crown of the tooth, and throughout Tomes' fibers and their secondary processes.

2. High concentrations of specific cholinesterase appeared at the dentino-enamel junction, probably due to the characteristic branching of Tomes' fibers in this area.

3. Specific cholinesterase is present in the extensions of Tomes' fibers (spindles) in enamel.

4. The areas of concentrations of specific cholinesterase correlate with the areas of clinical pain experience in teeth.

5. The mechanism of pain conduction is thus believed to be along Tomes' fiber to its cell body, the odontoblast, at which point there is a synapse with the adjacent free nerve endings. These nerve endings conduct pain impulses to the larger pulpal nerve trunks which then exit through the apical foramina.

6. Although the odontoblast may function in neural impulse conduction, this does not necessarily preclude other functions that have been ascribed to this cell and its process.

7. Nonspecific cholinesterase is present in concentrated amounts in the blood vessels of the pulp, including the smaller vessels underlying the odontoblasts. Lesser amounts are present in the extracellular fluid of the pulp and in Tomes' fibers.

The authors wish to express their sincere appreciation to Miss Elizabeth Haley for her assistance in the preparation of the tissues and to Mr. Edward Crandall for the photomicrography.

REFERENCES

1. Nachmansohn, D.: Role of Acetylcholine in Conduction, Bull. Johns Hopkins Hosp. **83**: 463-496, 1948.
2. Elliott, T. R.: The Action of Adrenalin, J. Physiol. **32**: 401-467, 1905.
3. Loewi, O.: Ueber humoral ueber—Frag barkert der Herzneruenwerkung, Arch f. d. ges. Physiol. **189**: 239-242, 1921.
4. Dale, H. H. and Feldberg, W.: Chemical Transmission at Motor Nerve Endings in Voluntary Muscle, J. Physiol. **81**: 39, 1934.
5. Nachmansohn, D.: Chemical Mechanism of Nerve Activity, Ann. New York Acad. Sc. **47**: 395-428, 1946.
6. Burgen, A. S. V., and Chipman, L. M.: Cholinesterase and Succinic Dehydrogenase in Central Nervous System of Dog, J. Physiol. **114**: 296-305, 1951.
7. Plattner, F.: Der Nachweis des Vagusstoffes beim Säugetiere, Arch. ges. Physiol. **214**: 112-129, 1926.
8. Engelhart, E., and Loewi, O.: Fermentative Azetylcholinspaltung im Blut and ihre Hemmung durch Physostigmin, Arch. exper. Path. u Pharmakol. **150**: 1-13, 1930.
9. Mendel, B., Mundel, D. B., and Rudney, H.: Studies on Cholinesterase; Specific Tests for True Cholinesterase and Pseudo-cholinesterase, Biochem. J. **37**: 473-476, 1943.
10. Nachmansohn, D.: Transmission of Nervous Influx in Central Nervous System; Presence of Cholinesterase and Role of Acetylcholine, Compt. rend. Soc. de biol. **126**: 783-785, 1937.
11. Nachmansohn, D.: Cholinesterase in Nerve Fibers, Compt. rend. Soc. de biol. **128**: 516-519, 1938.
12. Nachmansohn, D.: Cholinesterase in Tissue of Nervous System, Compt. rend. Soc. de biol. **127**: 894-896, 1938.
13. Nachmansohn, D., and Marnay, A.: Cholinesterase in Voluntary Muscle, J. Physiol. **92**: 37-47, 1938.
14. Zajicek, J., Sylven, B., and Datta, N.: Attempts to Demonstrate Activity in Blood and Bone Marrow Cells by a Modified Thiocholine Technique, J. Histochem. **2**: 115-121, 1954.
15. Stedman, E., Stedman, E., and Easson, L. H.: Choline-esterase. Enzyme Present in Blood Serum of the Horse, Biochem. J. **26**: 2056-2066, 1932.
16. Milhorat, A. T.: Activity of Serum in Disease, J. Clin. Invest. **17**: 649-657, 1938.
17. Koelle, G. B.: Elimination of Enzymatic Diffusion Artifacts in Histochemical Localization of Cholinesterase and Survey of Their Cellular Distributions, J. Pharmacol. & Exp. Therap. **103**: 153-171, 1951.
18. Koelle, G. B.: Cholinesterase of Tissues and Sera of Rabbits, Biochem. J. **53**: 217-226, 1953.
19. Augustinsson, K. B., and Nachmansohn, D.: Distinction Between Acetylcholine-esterase and Other Choline Ester-Splitting Enzymes, Science **110**: 98-99, 1949.

20. Koelle, G. B., and Friedenwald, J. S.: Histochemical Method for Localizing Cholinesterase Aetivity, Proc. Soc. Exper. Biol. & Med. **70**: 617-622, 1949.
21. Pearse, A. G. E.: Histochemistry (Theoretical and Applied), Boston, 1953, Little, Brown & Company, pp. 465-467.
22. Churchill, J. A., Schuknecht, H. F., and Doran, R.: Acetylcholinesterase Activity in the Cochlea, Laryngoscope **66**: 1-15, 1956.
23. Avery, J. K., and Rapp, R.: Demonstration of Cholinesterase in Teeth, Stain Technol. **33**: 31-37, 1958.
24. Bernick, Sol.: Innervation of Teeth and Periodontium After Enzymatic Removal of Collagenous Elements, ORAL SURG., ORAL MED. & ORAL PATH. **10**: 323-332, 1957.
25. Rapp, R., Avery, J. K., and Rector, R. A.: A Study of the Distribution of Nerves in Human Teeth, J. Canad. Dent. A. **23**: 447-453, 1957.
26. Brashear, A. D.: The Controversy Concerning the Innervation of the Teeth, J. D. Res. **16**: 5-17, 1937.
27. Koelle, G. B.: Histochemical Differentiation of Types of Cholinesterase and Their Localizations in Tissues of Cat, J. Pharmacol. & Exper. Therap. **100**: 158-179, 1950.
28. Koelle, G. B.: Cholinesterases of the Central Nervous System, J. Neuropath. & Exper. Neurol. **14**: 23-27, 1955.

ORAL PATHOLOGY

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THE AMELOBLASTOMA AND THE CRANIOPHARYNGIOMA—THEIR SIMILARITIES AND DIFFERENCES

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THE craniopharyngioma has been called the pituitary ameloblastoma, and not without justification. The two are not exactly alike, however, and certain microscopic criteria may be employed to separate the pituitary from the jaw neoplasm in the vast majority of cases.

Craniopharyngioma has been called by a large number of names, the more common being Rathke's pouch tumor, suprasellar cyst, hypophyseal duct tumor, and cranial adamantinoma.[1, 3] It has been believed that the tumor arises from the epithelial cell rests of the craniopharyngeal canal. This latter represents the path taken by Rathke's pouch, the evagination of the stomadeum that fuses with an outgrowth of the diencephalon forming the pituitary gland.

During embryonic life, about the time of tooth germ initiation, the epithelial cells rostral to the oral plate proliferate and extend upward and backward to contact with a diencephalic downgrowth around which they partially wrap themselves. The connection with the oral cavity degenerates much as does the dental lamina by the third intrauterine month, although in a small percentage of newborn infants this craniopharyngeal canal persists. At about the tenth week there is a marked cellular proliferation in the ventral pouch forming the anterior lobe. The epithelial cell rests, which result from degeneration of the duct and initially lie on the anterior wall, are pushed superiorly and finally come to rest in the region of the hypophyseal stalk. Thus, a craniopharyngioma may arise at any point from the posterior nasopharynx to the floor of the third ventricle of the brain.[4] These tumors are even noted

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This study has been made possible through a grant from the United States Public Health Service.

occasionally to occur within the body of the sphenoid bone.[2] Difficulty arises because these cell rests are not usually found in young persons, whereas craniopharyngioma occurs principally in young persons, so that the ultimate origin of these tumors is still hotly debated.

More recently another theory of origin has been expressed by Biggart,[5] Carmichael,[4] and Kernohan and Sayre,[6] namely, that the "cell rests" are not of embryonic origin but are possibly metaplastic cells of hypophyseal origin.

Although the craniopharyngioma may occur at any age, the vast majority of these tumors are found in infants, children, and young adults who have not reached the age of 25 years. Bailey and associates,[1] in a survey of 138 examples of this tumor, reported that two-thirds occurred within the first three decades of life. Love and Marshall,[7] surveying 100 cases, confirmed this impression, stating that more than one-half of the patients were below 10 years of age. This is in contrast to the jaw tumor that has its peak incidence between the third and fourth decades. There appears to be no sex preference with regard to either tumor.

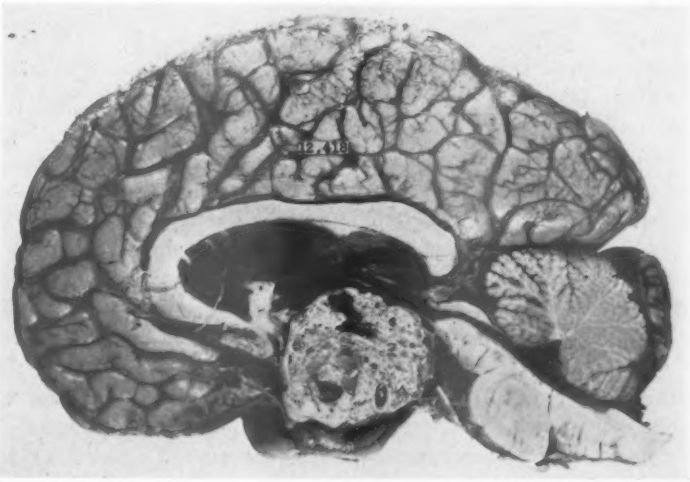

Fig. 1.—Sagittal section of brain showing involvement of midbrain with craniopharyngioma. Note numerous cystlike spaces within the tumor, extension through the floor, and invasion of the third ventricle.

Most craniopharyngiomas are grossly cystic (Fig. 1). In the ameloblastoma, although microscopic cysts are noted, large fluid-containing cystic areas are not usually found. Calcified masses are very commonly found in the craniopharyngioma and occasionally metaplastic bone or cartilage is formed. Love and Marshall found that 77 per cent of their cases had microscopic calcified areas. However, the amount was insufficient in some cases to produce diagnostic radiopacity under x-ray. The ameloblastoma does not contain calcified material; nor does it manifest metaplastic bone formation.

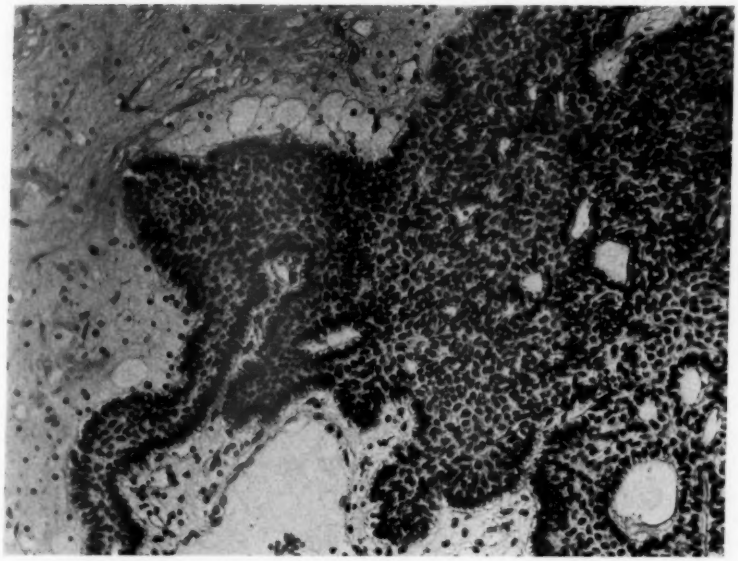

Fig. 2.—Histologic section of Case 3. Note typically palisaded basal cells. A delicate connective tissue base separates the epithelial tissue from the mucoid-appearing tissue. (Magnification, ×125; reduced 1/10.)

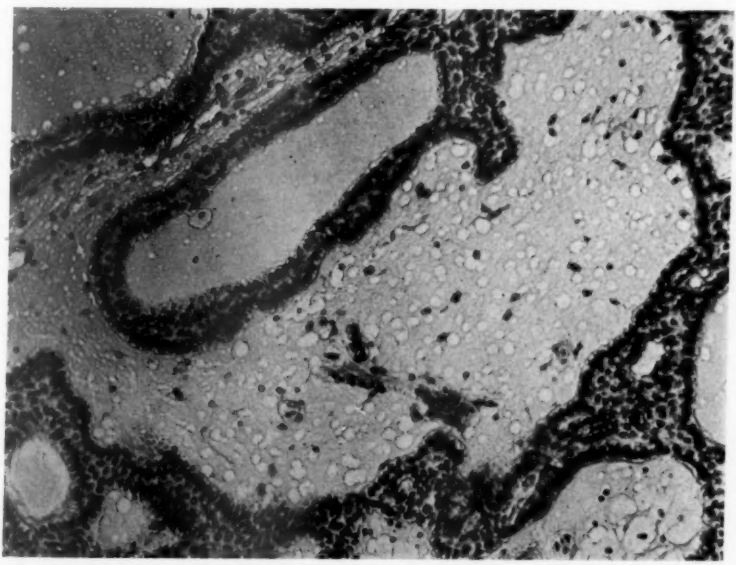

Fig. 3.—Note the strandlike appearance of some areas of the tumor seen above. The resemblance to dental lamina is marked. (Magnification, ×125; reduced 1/10.)

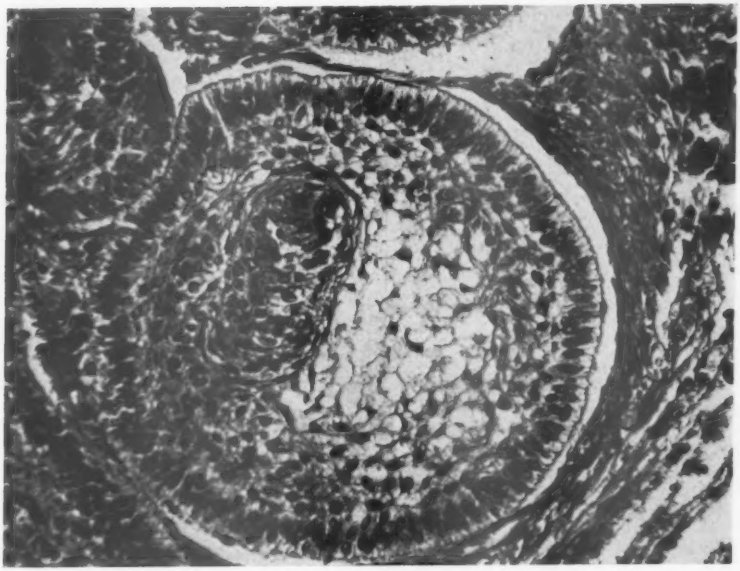

Fig. 4.—Case 5. High-power view demonstrating the arrangement of the basal cells to the connective tissue basement membrane. Note polarity of nuclei away from the membrane. Note also the acanthomatous tendency, and the tendency of the stellate areas to break down with resultant cyst formation. (Magnification, ×415; reduced 1/10.)

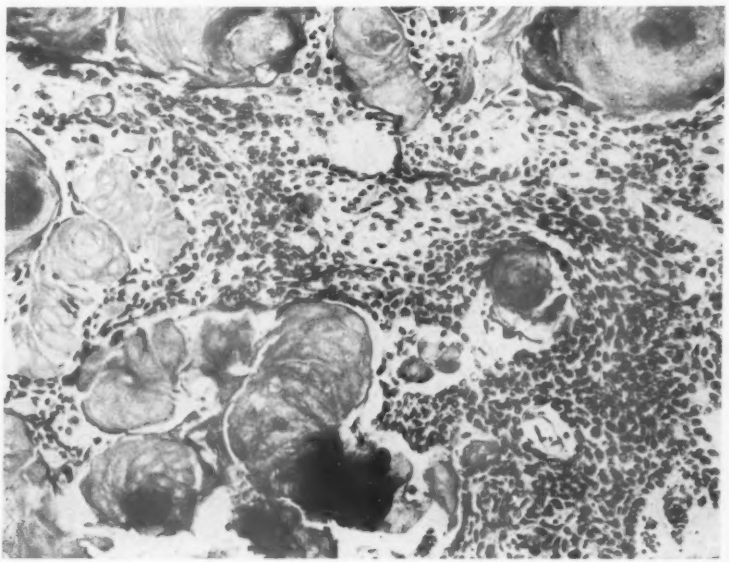

Fig. 5.—Note masses of cornified "ghost epithelium." These masses become calcified epithelial masses to tumor. (Magnification, ×125; reduced 1/10.)

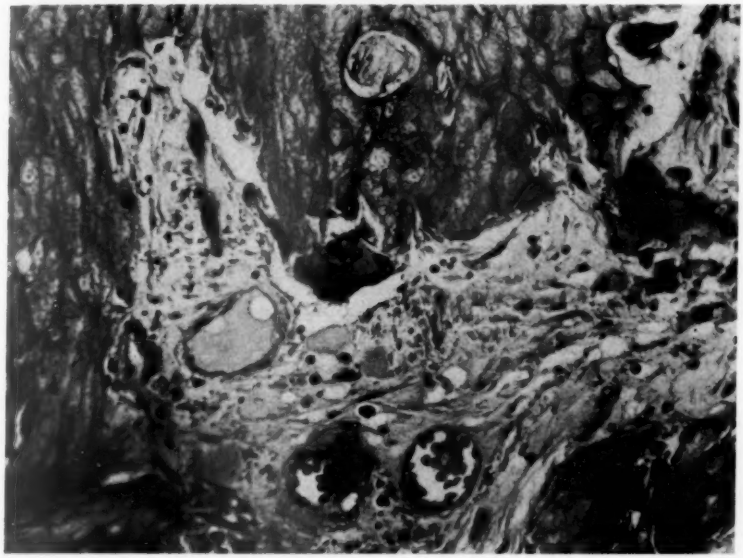

Fig. 6.—Higher-power view of case seen in Fig. 5. Note foreign body giant cell at edge of cornified epithelial mass. (Magnification, ×415; reduced 1/10.)

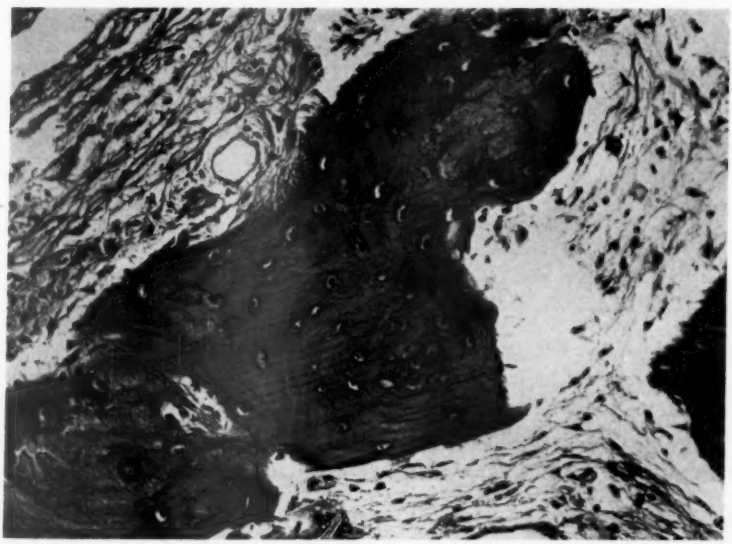

Fig. 7.—Bone. In a number of craniopharyngiomas bone or even cartilage is formed. Cornified epithelial tissue is to be noted at lower left. (Magnification, ×415; reduced 1/10.)

TABLE I

CASE	AGE OF ONSET OF SYMPTOMS	SEX	CALCIFICATION	OSSIFICATION	GROSS APPEARANCE
1	5	M	Yes	Cartilage	Cystic
2	1	M	Yes	0	Cystic
3	7	F	Yes	0	Cystic
4	5	M	Yes	Osteoid	Cystic
5	12	M	Yes	Bone	Cystic
6	24	M	Yes	0	Cystic
7	38	M	Yes	0	Cystic
8	6	F	Yes	Bone	Cystic
9	26	F	Yes	0	Cystic
10	36	M	Yes	0	Cystic
11	39	M	Yes	0	Cystic
12	7	F	Yes	Bone	Solid
13	7	F	Yes	0	Cystic
	X = 16.4	M = 8 F = 5	Yes = 13 No = 0	Cartilage 1 Bone or osteoid 4 Neither 8	Cystic 12 Solid 1

The craniopharyngioma is commonly encapsulated, although brain invasion occurs not uncommonly. On the other hand, only about one-half of the ameloblastomas are encapsulated (Table II).

Microscopically, there is considerable similarity between the two tumors. In the hypophyseal tumor, strands of columnar epithelium, remarkably similar to dental lamina, are observed. A stellate reticulum is also frequently, but by no means constantly, present for these cells degenerate, forming cysts, or they undergo metaplasia to masses of squamous epithelial cells that cornify.

TABLE II

	AMELOBLASTOMA	CRANIOPHARYNGIOMA
Age	Third and fourth decades	First and second decades
Gross appearance	Cystic and solid	Predominantly cystic
Encapsulation	About half	Commonly encapsulated
Microscopic	No calcification No metaplastic bone formation	Calcification very common; occasional bone or, rarely, cartilage formation
Response to hi-voltage roentgen therapy	Little to none	None

These areas of keratinization undergo calcification. Foreign-body giant cells may be seen about the edges of these calcified masses or about the cholesterol clefts that are commonly present (Figs. 2 to 7).

Thirteen cases of craniopharyngioma were surveyed from the files of the pathology department. The results are summarized in Table I.

REFERENCES

1. Bailey, P., Buchanan, D. N., and Bucy, P. C.: Intracranial Tumors of Infancy and Childhood, Chicago, 1939, University Chicago Press.
2. Zeitlin, H.: Adamantinomas of Hypophyseal Stalk and Sphenoid Bone, Am. J. Cancer **23**: 729, 1935.

3. Critchley, M., and Ironside, R. N.: The Pituitary Adamantinomata, Brain 49: 436, 1926.
4. Carmichael, H. T.: Squamous Epithelial Rests in the Hypophysis Cerebri, Arch. Neurol. & Psychiat. 26: 966, 1931.
5. Biggart, J. H.: Pathology of the Nervous System; A Student's Introduction, ed. 2, Baltimore, 1949, Williams & Wilkins Company.
6. Kernohan, J. W., and Sayre, G. P.: Tumors of the Pituitary Gland and Infundibulum, Fascicle 36, Washington, 1956, Armed Forces Institute of Pathology.
7. Love, J. G., and Marshall, T. M.: Craniopharyngiomas (Pituitary Adamantinomas), Surg. Gynec. & Obst. 90: 591, 1950.

TRANSITIONAL-CELL CARCINOMA OF THE MAXILLARY SINUS

Report of a Case

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MALIGNANT tumors of epithelial origin that may occur in the oral cavity are squamous-cell carcinoma, adenocarcinoma, basal-cell carcinoma, and transitional-cell carcinoma. Squamous-cell carcinomas are the most common tumors of epithelial origin found in this region. Basal-cell carcinoma is rare, its usual site being the face or lips. The transitional-cell carcinoma is commonly seen in the oropharynx and nasopharynx. It is sometimes found in the maxillary sinus, from which it may invade and involve the hard palate, producing a lesion in the mouth. From the standpoint of the dental surgeon, its presence must be considered in making a differential diagnosis of a malignant tumor. Its early recognition and treatment are essential because of its grave prognosis due to the early widespread formation of metastases.

CASE REPORT

A 48-year-old man was referred to the department by his medical advisor. The patient complained of pain of two months' duration in the left upper alveolus. He also complained of an ulcer in this region but could not say when it first appeared.

Examination.—There was slight puffiness of the left cheek, and the left upper deep cervical nodes were palpable. The patient was edentulous. There was a large area of erythema on the left side of the hard palate, extending posteriorly to the junction of the hard and soft palate and laterally over the ridge in the molar region. This area was not raised, except for a small area anteriorly; nor was it indurated. In the second molar region there was a deficiency in the alveolar ridge, and this area was occupied by an ulcer, about 1 cm. in diameter, covered with a grayish slough (Fig. 1).

The patient was experiencing a continuous dull ache from the region; this periodically became severe and radiated along the infraorbital nerve and down into the neck. Analgesics did not relieve the pain.

There had been no discharge from the nose and no epistaxis, but the patient stated that the left nostril had been obstructed for some time. His appetite was good, but he was not sleeping well. There was no relevant medical history.

Investigations carried out included x-ray pictures of maxillary sinuses and chest, dental films of the $\underline{|678}$ region, and biopsy of the ulcer.

X-ray Reports.—The films of the maxillary sinuses showed that the anterior and posterior walls of the left antrum were normal. However, a larger film showed that the roof of the left antrum was abnormal as was its junction with the lateral wall, where the bony

From the Department of Oral and Dental Diseases, Crumpsall Hospital, Manchester, England.

outline was actually absent, except for the inner end of the roof (Fig. 2). In the left antrum there was a thick and dense mucosal swelling which ended abruptly in a rather unusual way near the inner aspect of the antral roof. These points suggested that the mucosal swelling, or part of it, may have originated from something other than a chronic

Fig. 1.—Ulcer in $\underline{|7}$ region.

Fig. 2.—Occipitomental view of maxillary sinuses.

infection. The possibility of an early-stage neoplasm of the antral mucosa had to be borne in mind. The intraoral roentgenogram (Fig. 3) showed an irregular radiolucent area in the region discussed. Films of the chest revealed no abnormalities.

Biopsy.—Under local anesthesia, a biopsy specimen of the ulcer was obtained and sent for histologic examination.

Pathologist's Report.—This is a tumor of the basal-cell carcinoma type, showing no definite affinity with salivary gland tumors or squamous carcinoma. The cells form solid rounded masses, the outermost layer tending to low columnar shape in some places. The cells tend to be of uniform size and staining, and only occasional mitoses are seen (Figs. 4 and 5).

Diagnosis: Basal-cell carcinoma.

In view of this report, the patient was referred to the Christie Hospital and Holt Radium Institute in Manchester, England. The Christie Hospital pathologist was of the opinion that this tumor was a transitional-cell carcinoma, probably arising from the mucous gland ducts, and not a basal-cell carcinoma.

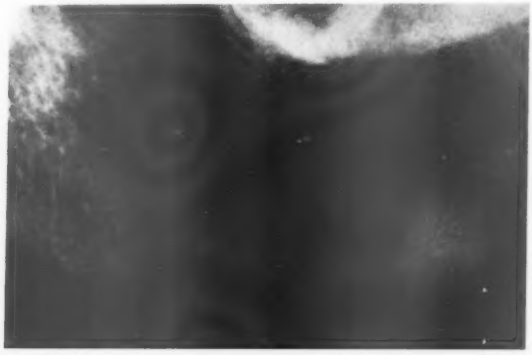

Fig. 3.—Intraoral roentgenogram of $\underline{|67}$ region.

The primary lesion was treated by means of a radium implant in the left antrum. Ten weeks later the mouth and antrum appeared to have healed well, and a block dissection of the left side of the neck was performed to remove large secondary nodes. These nodes were sent for section and yielded a similar report of transitional-cell carcinoma.

The block scar healed uneventfully.

Twelve months later progress was not satisfactory, as there was a recurrence in the area of the block dissection. Recurrent nodes were excised and were reported as showing transitional-cell carcinoma. These secondary nodes became rampantly recurrent, and a stage was reached where no further treatment could be undertaken.

DISCUSSION

Mucous membranes of certain parts of the body are covered with epithelium which does not keratinize. Carcinomas arising from these positions fail to show the characteristics of the squamous-cell type. These tumors, however, grow more rapidly and are more malignant. They are known as transitional-cell carcinoma and are often classified with lymphoepithelioma.

When the tumor is purely epithelial in type, it is referred to as a transitional-cell carcinoma, whereas with the lymphoepithelioma there is usually a marked intermingling of epithelial cells and lymphocytes derived from the underlying lymphoid tissue.

These tumors occur in the posterior part of the oral cavity, the nasopharynx, and the maxillary sinus. From the latter site they may break

through the hard palate into the mouth. When the tumor is situated in the nasopharynx, diagnosis is difficult because of its inaccessibility. The maxillary sinus is a common site for this tumor, and its possible presence should be borne in mind in the case of differential diagnosis of tumors of the antrum.

Microscopically, the cells are large and pale with indefinite outlines. Frequently they show a tendency to epithelioid differentiation, and frequently

Fig. 4.

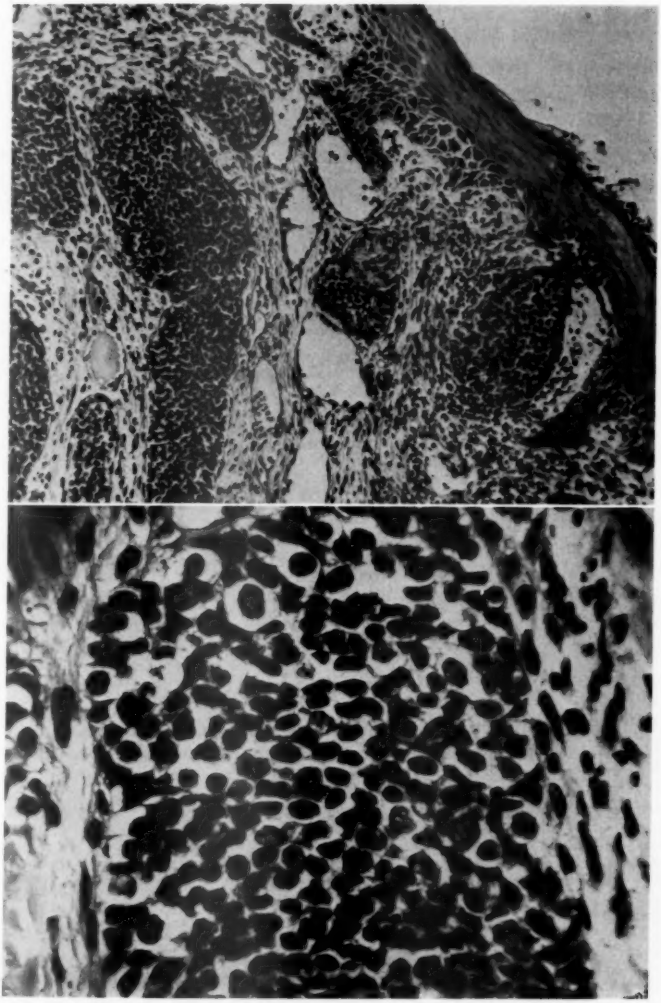

Fig. 5.

Fig. 4.—Low-power view of tumor. (Magnification, approximately ×120.)
Fig. 5.—High-power view of tumor cells. (Magnification, approximately ×500.)

they are arranged in sheets. Sometimes the cells may be arranged in strands and closely related with lymphoid tissue when it is described as a lymphoepithelioma. The nuclei are large and deeply staining and contain various amounts of chromatin; Boyd states that mitoses are numerous. There may be a tendency toward differentiation with squamous characters appearing, or toward anaplasia, so that differentiation from anaplastic forms of epidermoid tumors and reticulum-cell sarcoma may be difficult. In lymphoepithelioma, however, the reticulum is generally deposited in coarse fibers associated with stroma and blood vessels, while in the reticulum-cell sarcoma the fibrils are fine and closely related to the tumor cells.

Transitional-cell carcinoma is highly malignant, and although the primary growth may be small, metastatic spread to the regional glands is early and widespread. Visceral spread to the lungs and liver may occur at a later date.

The primary lesion responds to irradiation, but the prognosis is very grave because of the early formation of metastases which may assume massive proportions.

The difference in opinion of the pathologists in this case is interesting. Thoma reports that in basal-cell carcinoma of the oral mucosa the tumor cells resemble the basal cells of the oral epithelium. The peripheral cells are arranged in a columnar fashion, and no evidence of keratinization is present.

Histologically there is a definite resemblance of the material obtained from this case to that of a basal-cell carcinoma. The origin of this tumor in the maxillary antrum and the formation of metastases in the regional lymph nodes, however, preclude the belief that the tumor could have been a basal-cell carcinoma.

SUMMARY

A case of transitional-cell carcinoma of the maxillary sinus involving the hard palate is reported. The site of occurrence, the histology of these tumors, and the difficulty of their diagnosis are discussed. Their grave prognosis because of metastases which recurred following a block dissection of the neck is illustrated in the case presented.

I am indebted to Mr. W. C. Mellor for permission to publish this case and also thank the Department of Medical Illustration, Crumpsall Hospital, for producing the photographs.

REFERENCES

1. Bernier, J. L.: Oral Surg., Oral Med. & Oral Path. 2: 690, 1949.
2. Thoma, K. H.: Oral Pathology, ed. 3, London, 1950, Henry Kimpton.
3. Boyd, W.: Textbook of Pathology, ed. 5, London, 1947, Henry Kimpton.

ENDODONTICS

INFLAMMATORY POTENTIAL OF ROOT CANAL MEDICAMENTS

A Preliminary Report Including Nonspecific Drugs

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INTRODUCTION

PAIN or discomfort occasionally follows routine endodontic procedures. In the absence of periodontal complications, this discomfort is probably the result of one of three vectors or a combination of them: infection, improper instrumentation, and improper medication. This study is directed at an analysis of the role of medication in producing pain in root canal therapy.

Endodontic medicaments will be defined as agents which are used within the pulp chamber and root canals for purposes of irrigation, sterilization, and amelioration of pain or other untoward symptoms. Injectable local anesthetics, rubber dam sterilizing agents, and drugs taken systemically have not been considered significant in initiating pulpal or periapical pain and have not been included in these investigations.

Drugs can cause pain only if they are irritating per se, and then only if they are allowed to contact tissues which can be inflamed by them. For example, isotonic saline is non-irritating to the tissues for which it is isotonic; it can contact these tissues without causing inflammation or pain. On the other hand, sulfuric acid is irritating to most organic tissue. If sulfuric acid could

This study was presented in partial fulfillment of the research requirements for the teaching research fellowship in endodontics at Temple University for the year 1955-1956. It represents work begun at Temple University and completed at Beth Israel Hospital in Boston.

This preliminary report was read at the annual session of the American Association of Endodontists in Chicago, Illinois, in February, 1957.

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be used therapeutically without contacting the tissues for which it is an irritant, it, too, would cause no irritation or pain. If the acid contacted these tissues, however, pain would ensue.

There is, therefore, an irritant potential to many drugs, irrespective of their manner of use. This irritant potential is of great importance in the practice of clinical endodontics.

A further analysis of the role of medicaments in producing pain shows that two factors are involved: (1) the irritant potential of the drug itself and (2) the manner of its use. The method by which a drug is used in root canal therapy determines the tissues that it contacts and the quantities of the drug that are applied to these tissues. This latter factor, the manner in which the drug is used, has been extensively discussed in texts on endodontics. The irritant potential of the drugs themselves has received relatively little attention.

Many clinicians, sensing perhaps that most drugs are capable of irritating periapical tissues, strongly suggest that the use of medicaments be limited to the confines of the pulp chamber and root canals.[1-4] Since the source of bacterial and chemical irritants in endodontic problems is in the root canals and not the periapical tissues, this clinical admonition to keep drugs from passing beyond the root apex is sound bacteriologically,[5, 6] and histopathologically[7] as well. While wholly desirable, such limitation of instrumentation and medication within the confines of the root canals cannot always be achieved. A greater knowledge of the properties of the drugs that we use seems to be in order.

OBJECTIVE

This study is concerned with the extent to which the various medicaments used in root canal therapy can cause inflammation in tissues. Under ideal clinical management, these drugs should be confined to the root canal and should not come in contact with the periapical tissues. In actual practice, however, acute periapical inflammations do occur from time to time as the result of overmedication or improperly directed medication. In these cases, the drug has passed beyond the apical foramen and acts as an irritant in the periapical tissues.

It would seem desirable to know the inflammatory potential of the various drugs. With this information available, it should be possible, at a later date, to weigh the antimicrobial effectiveness of each medicament against its inflammatory potential. Much more accurate data are available at the present time concerning the measurable antiseptic qualities of these drugs[8-10] than exists concerning their action as irritants. Knowledge of their inflammatory potential might lead to a more rational use of drugs in root canal therapy.

METHOD

In this study, mammalian soft tissue was used to determine the irritant potential of the drugs. Rabbits have long been the animals of choice for this

type of work. They are readily available and are almost immune to surgical infection. They have been used in carefully described inflammation studies which are adaptable to our work.[11-16]

Twelve common medicaments were tested: Cresatin, camphorated parachlorophenol, formocresol, eugenol, PBSC, Azochloramid, hydrogen peroxide 3 per cent, 5 per cent sodium hypochlorite solution (NaOCl), Zephiran chloride 1:1,000, beechwood creosote, silicone fluid (vehicle for PBSC), and distilled water.

Sterile physiologic saline was used as a control. PBSC, a much used polyantibiotic paste (Grossman) containing penicillin, bacitracin, streptomycin, and caprylate sodium in a silicone base, was included to represent the class of polyantibiotic preparations.[10] All the other drugs represent a class of medicaments known as nonspecific root canal disinfectants.[2]

Two portions of the rabbit—abdominal integument and eyes—served as test areas.

Skin Studies.—In the skin studies, two procedures were employed:

1. One was the intradermal injection of 0.1 c.c. of each drug into the skin on the shaved abdomens of male white rabbits of 3,000 grams minimum weight. The use of male rabbits, while not essential, reduces the possibility of cutting the nipples during shaving. Shaving was accomplished first with graded electric clippers and completed with a straight razor. If any irritation was apparent at this time, the animal was not used until the following day. Great care had to be taken to make the injections intradermal, producing a wheal, and not subcutaneous.

Skin observations were made after twenty-four hours. Frequently the lesions were allowed to mature for three days, after which further observations were made.

2. A refinement of the skin technique was employed by introducing a vital dye, trypan blue, into the blood stream of the animal. This is done by following the intradermal injections with the introduction of 6 c.c. of a saturated solution of trypan blue into the long veins of a shaved ear. The intravenous injection is performed one-half to one and one-half hours after those made by the intradermal route. Since increased capillary permeability is one of the earliest tissue changes in inflammation, the blue dye will rapidly accumulate around an irritant, illustrating the phenomenon of inflammatory localization.[17, 18] The quantity and intensity of the blue area localizing at the site of the original intradermal injection indicate the severity of the inflammation. These tissues can also be biopsied and the dye particles counted microscopically. Eventually, the entire animal turns blue and remains so for about six weeks.

Eye Studies.—In the eye studies, 0.15 c.c. of each drug was introduced into the eye of a rabbit by drawing the lower lid out slightly and depositing the material into the conjunctival sac. Physiologic saline, 0.15 c.c., was introduced into the opposite eye as a control. The lids were gently pressed together for one

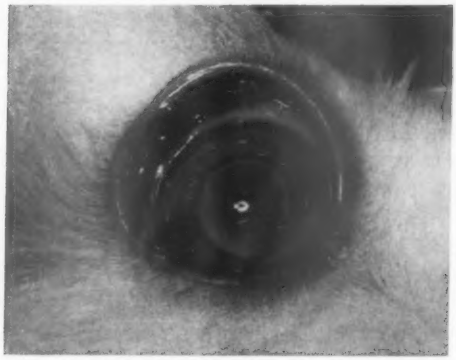

Fig. 1.—Control (physiologic saline).

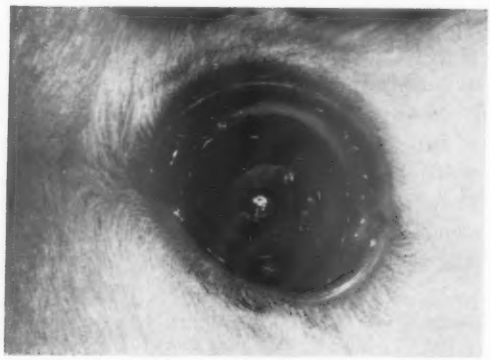

Fig. 2.—Cresatin.

Fig. 3.—Camphorated parachlorophenol.

Figs. 1 to 6.—Rabbit eyes three to four hours after the introduction of 0.15 c.c. of drug into conjunctival sac.

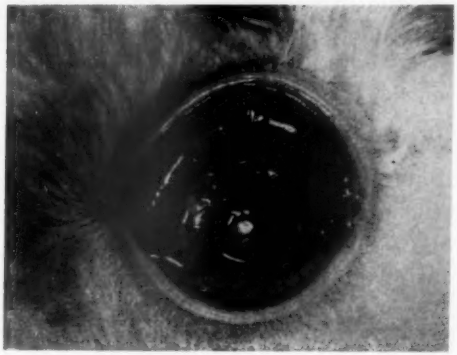

Fig. 4.—Formocresol.

Fig. 5.—PBSC.

Fig. 6.—Beechwood creosote.

minute to ensure adequate retention of the drug, and observations were then made in three to five minutes. Further observations were made in three to four hours, one day later, two days later, and occasionally after five-day periods.

The most reproducible results seemed to be observed in the three- to four-hour eyes. This period of time seemed necessary to give a maximum effect after repeated trials. Longer periods of time led to experimental complications related to rates of healing.

Observations included six general factors:

1. Swelling of conjunctiva.
2. Hyperemia of conjunctiva—redness.
3. Etching or clouding of the cornea.
4. Loss of clarity of fine anatomic marks normally visible in the iris.
5. External swelling.
6. Exudation.

Observations were taken from the living animal in all cases, and not from Kodachrome slides which, while useful, occasionally miss a pertinent factor due to photographic difficulties.

RESULTS

The results of the skin studies are summarized in Table I.

TABLE I. OBSERVATIONS ONE DAY FOLLOWING INTRADERMAL INJECTION OF 0.1 C.C. OF DRUG

Severely Inflamed
Beechwood creosote
Azochloramid (1:500 in triacetin)
Camphorated parachlorophenol
Eugenol
Formocresol
Chlorinated soda (double strength)
Slightly Inflamed
Cresatin
PBSC
No Inflammation
Distilled water
Silicone fluid (DC 200)
Zephiran (1:1,000)
Hydrogen peroxide (3%)

Note: In every animal, intradermal injection of physiologic saline gave no evidence of inflammation.

Since PBSC is a paste, it was necessary to dilute the material in an equal volume of silicone fluid (DC 200), the recommended vehicle for its antibiotic constituents.

The medicaments fell into three easily discernible categories. It was found that the drugs which accumulated the greatest quantity of dye in the shortest period of time also displayed the severest reactions when no vital stain was used.

Biopsies were made from the animals that received the vital stain soon after the stain accumulated. In the animals that did not receive trypan blue injections, the lesions were allowed to mature and observations were made daily.

The histologic sections were examined by the Department of Experimental Pathology at the Temple University Medical School, where minute differences in the degree of inflammation were noted. Those small differences, compared to the obvious differences observable grossly, limited the significance of the slides.

The results of the eye studies are summarized in Table II.

TABLE II. RESULTS OF EYE STUDIES

THREE TO FOUR HOURS AFTER INTRODUCTION OF 0.15 C.C. OF DRUG INTO CONJUNCTIVAL SAC	ONE DAY LATER
Severely Inflamed	
Beechwood creosote	Inflammations continued
Azochloramid (1:500 in triacetin)	
Camphorated parachlorophenol	
PBSC	
Eugenol	
Formocresol	
Moderately Inflamed	
Chlorinated soda (double strength)	Inflammations continued
Hydrogen peroxide (3%)	
Slightly Inflamed	
Zephiran (1:1,000)	Normal
No Inflammation	
Distilled water	Normal
Cresatin	
Silicone fluid	

Note: In every animal, the control eye, into which physiologic saline had been introduced, showed no evidence of inflammation.

The accumulated data were examined by the Ophthalmology Department of the Temple University Medical School, where it was decided that four categories of reaction were exhibited but that no numerical values could be assigned to the individual drugs within any one category.

DISCUSSION

Inflammation in this study is considered to be the reaction of tissues of higher animals to an injurious stimulation or irritant.[18] It varies from a barely perceptible reaction, or hyperemia, to the production of pus, or suppuration.

On a cellular level, the phenomenon of inflammation varies little from tissue to tissue or from animal to animal among the higher species. Cellular changes take place as a result of the presence of the irritant, and well-known vascular events are observed[19]:

1. After transitory constriction, capillaries in the inflamed area dilate.

2. Momentary acceleration of the flow of blood in the area is followed by marked slowing of the blood stream.

3. Margination, in which the leukocytes move from the axial stream to the peripheral zone of the capillaries, is observed.

4. Soon plasma and white blood cells permeate the capillary lining, contributing to the inflammatory exudate. Then the ameboid

movement of the white blood cells through the capillary wall, or diapedesis, occurs. These vascular changes, of course, are well known and have been observed in the same sequence in all animals.

The biochemical phenomena in inflammation have also been observed in many higher animals. Menkin[17] describes the following chemical factors after assaying samples of inflammatory exudate taken from any higher animal regardless of the site of inflammation or the nature of the irritant: leukotaxine, leukocytosis-promoting factors, necrosin, pyrexin, glucose, and growth-promoting factors. These chemical entities have been crystallized and, upon injection into another animal, will produce some particular characteristic of the inflammatory response.

It is unnecessary to record in this article the details of the cellular changes for which each of the isolated chemical factors is responsible. Also, we are not discussing the characteristic pH changes which are observed in all inflammatory tissues.[17] It should be clear, however, that although the symptoms of inflammation may vary slightly, depending on the tissues in which it is found, the basic elements of inflammation are the same regardless of the animal or area chosen for study.

The universal characteristics of inflammation have led many investigators to use undifferentiated connective tissue for their studies of cellular reactions. Likewise, the common elements involved in inflammation have led medical and pharmaceutical researchers to use the rabbit's eye for screening drugs when the irritant potential of the medicament was to be determined.[11-16] These areas are easy to handle, easy to observe, and have given consistent results.

Although certain advantages might be obtained by testing the root canal medicaments in periapical bone, certain disadvantages attend comparative studies of that type. Innumerable clinical variables were eliminated by testing the drugs in undifferentiated connective tissue and in the eye. The two tissues also complement each other in degree of sensitivity to irritants, the connective tissue being somewhat resistant and the eye being extremely sensitive to inflammation.

As a consequence of the variables involved in clinical endodontics, the successful use of a drug does not prove that it is non-irritating. The skill of the dentist, the care taken in chemomechanical instrumentation, the presence or absence of infection, and the judiciousness with which root canal medication is applied all leave the validity of clinical studies of inflammation in doubt.

Since the purpose of this study is the basic one of determining the inflammation potential of the drugs themselves, analyses of results with clinical patients were not included. The results should not be interpreted, therefore, as a direct comment on the clinical effectiveness of any drug. Neither should it be implied that the role of drug therapy in endodontics is of paramount importance in successful root canal work, since chemomechanical cleansing and complete obturation of the canal are probably of greater significance.[4, 20]

Nonetheless, certain clear-cut observations may be made:

1. Several nonspecific root canal medicaments which have long been considered to be highly irritating showed high irritant potentials in both methods employed in the study. Included among these were formocresol, beechwood creosote, and Azochloramid.

2. In addition, two widely used root canal medicaments of proved clinical effectiveness exhibited very high irritant potentials, namely, camphorated parachlorophenol and PBSC. Therefore, it seems incorrect to speak of camphorated parachlorophenol as a non-irritating drug, although it may be described as non-irritating under conditions of good clinical use. The same could be said for PBSC. These findings seem to re-emphasize the admonition that root canal medicaments be confined to the root canal and kept away from the periapical tissues. It was also interesting that, although the vehicle for the antibiotics in PBSC was non-irritating, the total preparation was an irritant. Another study, undertaken to determine why PBSC was irritating and what could be done to correct this, will be reported in the near future.

3. The common dental anodyne, eugenol, was found to be highly irritating. This finding reminds us that anodynes have various modes of action and that pain relief is not synonymous with freedom from inflammation.

4. The commonly used irrigants, hydrogen peroxide and chlorinated soda, while possessing some irritant potential, cause less severe reactions than do most of the drugs sealed in root canals between visits.

5. Several medicaments or agents—Zephiran chloride, cresatin, distilled water, and silicone fluid—showed little or no inflammation potential. Zephiran is occasionally used as a root canal irrigant,[21] and whatever its clinical advantages or disadvantages may be, it seems to be relatively non-irritating. Distilled water and silicone fluid are so non-irritating that no indication of their presence remains at the site of intradermal injection as soon as the fluid diffuses out of the wheal.

6. Cresatin was the only widely used root canal medicament described in the literature as non-irritating[8] which proved to be so in our studies. This drug is the acetic acid ester of metacresol. Coolidge[8] described it as having a characteristic persistent spicy odor and as having an anodyne effect on living tissue. He observed it to be non-irritating on tissues in full strength, although he did not describe his testing methods. He used it in combination with benzine (a substance with little germicidal action alone) and found the solution to have a phenol coefficient of 0.75. He described it as a very satisfactory remedy in root canal treatment in spite of its mild antiseptic properties and attributed much of its effectiveness to its prolonged action, since the drug is not readily exhausted, and to its low surface tension. Others have reported on the clinical effectiveness of cresatin.[1, 4, 22] The low surface tension may permit the drug to penetrate inaccessible crevices and canals by its wetting action and its penetration of fats and oils. Coolidge found the surface tension of this drug to be 37.7, and we found samples to exhibit surface tension of 31 ± 5 dynes per centimeter.[23]

As a result of this study, cresatin has become the medicament of choice for dressings in root canals following vital extirpation and in all other root canals after the first negative culture has been obtained at the Temple University Dental School[24] and the Beth Israel Hospital.

SUMMARY

Injudicious use of root canal medicaments can be one of the factors responsible for posttreatment pain. Although many clinically effective drugs were reported as non-irritating, very little controlled work was available to substantiate these claims. It seemed desirable to know more about the properties of the drugs that we use and to couple our knowledge of their antimicrobial potency with information regarding their inflammatory potential.

In accordance with accepted medical and pharmaceutical methods, several nonspecific root canal drugs and irrigants were tested by placement in the undifferentiated connective tissue of rabbit integument and by deposition in rabbit eyes. One commonly used polyantibiotic paste, distilled water, and a commonly used vehicle were also studied.

Many nonspecific root canal drugs were found to be highly irritating, as was the polyantibiotic paste that was tested. Successful clinical use of these drugs does not prove them to be less irritating but re-emphasizes the fact that drugs can and should be kept from contacting periapical tissues. Commonly used irrigating solutions were found to be slightly irritating but considerably less so than most drugs placed in the root canals between visits. Zephiran chloride, distilled water, and cresatin exhibited little or no inflammation potential. Some observations were made concerning the desirable properties of cresatin.

REFERENCES

1. Grossman, L. I.: Root Canal Therapy, Philadelphia, 1955, Lea & Febiger; Irritating Potentiality of Root Canal Medicaments, Am. J. Orthodontics & Oral Surg. 30: 564, 1944.
2. Sommer, R. F., Ostrander, F. D., and Crowley, M. C.: Clinical Endodontics, Philadelphia, & London, 1956, W. B. Saunders Company.
3. Coolidge, E. D.: Endodontia, Philadelphia, 1950, Lea & Febiger.
4. Stewart, G. G.: Rational Root Canal Medication, Clin. North America, pp. 823-834, November, 1957.
5. Hedman, W. J.: An Investigation Into Residual Periapical Infection After Pulp Canal Therapy, Oral Surg., Oral Med. & Oral Path. 4: 1173-1179, 1951.
6. Grossman, L. I.: Bacteriologic Status of Periapical Tissue in 150 Cases of Infected Pulpless Teeth, J. D. Res. 38: 101, 1959.
7. Fish, E. W.: Bone Infection, J. Am. Dent. A. 26: 691, 1939.
8. Coolidge, E. D.: Studies of Germicides for the Treatment of Root Canals, J. Am. Dent. A. 16: 710-711, 1929.
9. Bender, I. B., and Seltzer, S.: Advantages and Disadvantages of the Use of Antibiotics in Endodontics, Oral Surg., Oral Med. & Oral Path. 7: 993, 1954.
10. Grossman, L. I.: Polyantibiotic Treatment of Pulpless Teeth, J. Am. Dent. A. 43: 265, 1951.
11. Menkin, V.: Studies of Inflammation. I. Fixation of Vital Dyes in Inflamed Areas, J. Exper. Med. 50: 171, 1929.
12. Menkin, V., and Menkin, M. F.: Studies on Inflammation. II. A Measure of the Permeability of Capillaries in Inflamed Areas, J. Exper. Med. 51: 285, 1930.
13. Menkin, V.: Studies on Inflammation. III. Fixation of a Metal in Inflamed Areas, J. Exper. Med. 51: 879, 1930.

14. Menkin, V.: Recovery of the Leukocytosis-Promoting Factor in Exudates of Rabbits, Proc. Soc. Exper. Biol. & Med. **64:** 448, 1947.
15. Menkin, V.: An Aspect of Inflammation in Relation to Immunity, Arch. Path. **12:** 802, 1931.
16. Killian, J. A.: Summary of Tests of Local Irritant Effects of Experimental Preparations of Bactine, Section II-B, Miles Laboratories, Inc., Elkhart, Ind., August, 1957.
17. Menkin, V.: Biochemical Mechanisms in Inflammation, Springfield, Ill., 1956, Charles C Thomas, Publisher.
18. Menkin, V.: Newer Concepts of Inflammation, Springfield, Ill., 1950, Charles C Thomas, Publisher.
19. Boyd, W.: A Textbook of Pathology, Philadelphia, 1954, Lea & Febiger.
20. Summary of Reports, Second International Conference on Endodontics, University of Pennsylvania School of Dentistry, Philadelphia, June, 1958.
21. Auerbach, M. B.: Personal Communication on Use of Zephiran Chloride as a Root Canal Irrigant, N. Y. University School of Dentistry, New York, July, 1958.
22. Dietz, V. H.: XP-7: A Universal Endodontic Medicament, ORAL SURG., ORAL MED. & ORAL PATH. **10:** 1317-1322, 1957.
23. Woodson, H. H., and Drake, E. M.: Determination of Surface Tension of Cresatin, Study Done for the Authors, Massachusetts Institute of Technology, Cambridge, March, 1958.
24. Parris, L. N.: Personal Communication on Clinical Use of Cresatin, Temple University School of Dentistry, Philadelphia, June, 1958.

53 BAY STATE RD.
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A NEW AND SUPERIOR ENDODONTIC BACTERICIDAL AGENT

Part II

E. James Best, D.D.S., B. Franklin Gurney, B.S., M.S.,** and Audrey Conlin, R.N.,*** Chicago, Ill.*

INTRODUCTION

SINCE the very inception of the science of endodontics, constant investigation has been conducted to develop new materials and techniques for use in the treatment of the exposed and degenerating pulp. With the introduction and standardization of newer instruments, the biomechanical preparation of the root canal can be accomplished in a minimum amount of time. Furthermore, simplified techniques for the filling of the root canal, such as those suggested by Sommer[1] and others,[2] allow the dentist the maximum of accuracy while using gutta-percha to fill and seal the root canal and apical foramen. The use of silver cones following the procedures formulated by Jasper[3] makes filling the multirooted tooth a routine endodontic accomplishment. However, sterilization of the root canal with the complete elimination of bacteria and microorganisms may, and many times does, consume the most time and greatest number of appointments of an endodontic program. In our opinion, this phase of treatment presents the greatest barrier to the general practitioner who attempts endodontics. Others maintain that instrumentation is most important.

The chemotherapeutic agents used in the treatment of infectious material in the root canal have been many and varied. For years the majority of dentists relied on the germicidal compounds, such as the phenolic preparations. Because of the inherent toxicity of these drugs, frequent periodontitis and periapical necrosis resulted. After such discouraging experiences as these, many dentists recommended extraction as the most practical treatment of the exposed or infected pulp.

Fortunately, in recent years the development of the endodontic bactericidal agents has made impressive advancements. The introduction of the antibiotic and polyantibiotic materials by Grossman[4-6] stimulated the dental profession once again to try a new remedy. Further development of bactericidal agents

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was marked with the advent of Benzylog by Casey, Gurney, and Rapp.[7] This drug was para-aminotoluene sulfonamide used as an impregnant in endodontic paper points and as a topically applied bactericidal agent.

From the extensive clinical experience gained in the investigation of Benzylog, we arrived at the following conclusions:

1. The use of an impregnated endodontic paper point was an ideal vehicle for the treatment of infection in the root canal.
2. The use of an aqueous solution of the drug, applied topically, enhanced the therapeutic activity of the impregnant.
3. Although para-aminotoluene sulfonamide possessed excellent antibacterial properties, there were certain root canal contaminants against which its action was limited.[8]

It was necessary, therefore, to improve this drug or to find another endodontic bactericidal agent which would overcome these deficiencies.

In a previous article[9] we have shown that if 5-nitro-2-methylfurfuryl ether is combined with para-aminotoluene sulfonamide, the therapeutic deficiencies of Benzylog are completely overcome as demonstrated by in vitro experiments.

In this article a clinical program for testing this new preparation, which we have elected to call Endo-cide,* is set forth and the results are reported accordingly.

CLINICAL INVESTIGATION

All teeth selected for this study were pulpless. Prior to selection, each tooth was examined with radiographs and tested with an electrical vitalometer. As many cases as possible with extensive periapical bone involvement and fistulous tracts were chosen, since, in our opinion, cases such as these would be a true clinical test of the effectiveness of the drug. The root canal was not filled until two consecutive negative cultures were obtained. The clinical testing program that we established to conduct this phase of the study was carried out in the following manner:

Appointment 1.—The tooth was isolated with the rubber dam and all carious areas and defective fillings were removed and filled with zinc-oxyphosphate or silicate cement. Plastic crown forms and stainless steel bands were adapted to all degraded teeth. The rubber dam was cleansed with tincture of Mercresin followed by an application of 70 per cent ethyl alcohol. Entrance into the pulp chamber was gained through the lingual surface of anterior teeth and the occlusal surface of posterior teeth. The coronal portion of the pulp was removed, and the canal was gently explored with a smooth broach. Wherever possible, irrigation of the root canal was attempted with the Endo-cide solution to facilitate the removal of soft necrotic pulpal debris. The canal was then dried with sterile paper points. A dry Endo-cide point was inserted into the canal so that the tip did not extend beyond the apical foramen. The butt

*Endo-cide will be made available by the Novocol Chemical Mfg. Co., Inc., Brooklyn, New York.

end of the point was moistened with Endo-cide solution, over which was placed a pellet of cotton to act as a reservoir for the solution. A double seal of temporary stopping and zinc-oxyphosphate cement was used to close the tooth.

Appointment 2.—The tooth was isolated with the rubber dam, which was cleansed with tincture of Mereresin followed by an application of 70 per cent ethyl alcohol. With sterile instruments, the dressing was removed and the canal was thoroughly dried with sterile paper points. A sterile paper point was inserted into the canal and a bacterial sample was taken. The culture point was then placed in a tube of brain-heart infusion broth and incubated for bacteriologic examination. The remainder of this appointment was utilized in obtaining the diagnostic radiograph and completing the biomechanical preparation. A dressing was inserted in the manner described for the first appointment.

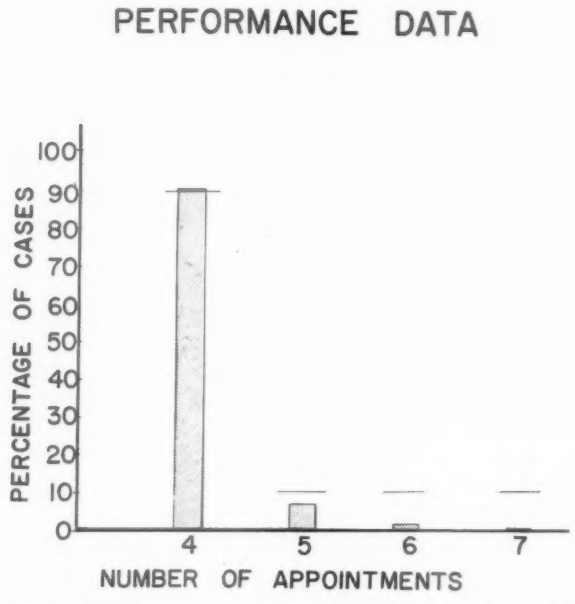

Fig. 1.—Clinical efficiency of Endo-cide. (See text for explanation.)

Appointment 3.—The second culture was taken at this appointment, and a new dressing was inserted. Sealing of the tooth was completed in the manner described in the initial appointment.

Appointment 4.—If two consecutive negative cultures were obtained, the root canal was filled with either gutta-percha or silver cones.

The culture medium used for all the cases in this study was brain-heart infusion broth. Bacteriologic examination was made at intervals of twenty-four, forty-eight, seventy-two, and ninety-six hours. If there were no visible

changes in the culture medium after ninety-six hours, the culture sample was deemed negative. Each case was treated in precisely the manner described in the foregoing paragraphs, with two consecutive negative cultures a prerequisite prior to filling the root canal. A total of 304 cases, of which 193 were anterior teeth and 111 were posterior teeth, were completed for this investigation. The results are shown in Fig. 1.

A demonstration of postoperative healing and repair is shown in Figs. 2 to 7.

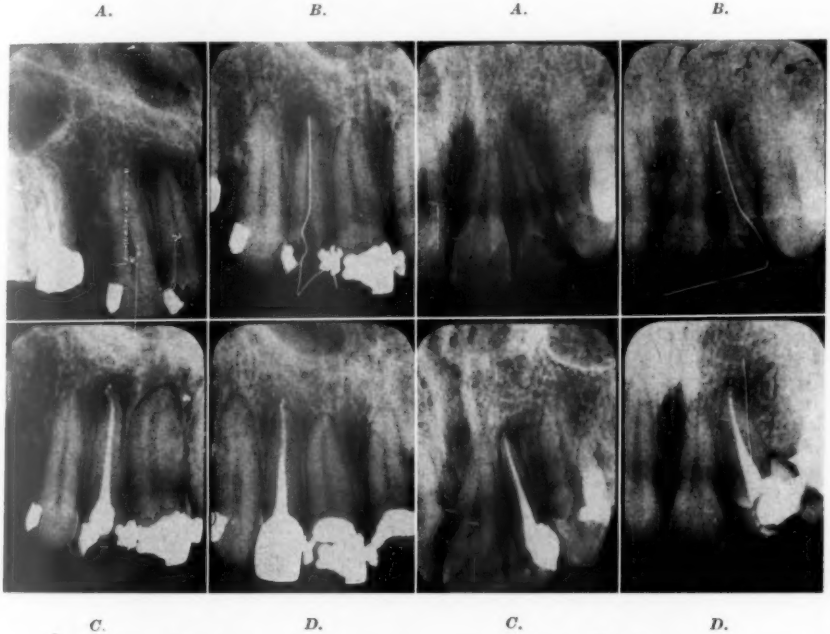

Fig. 2.

Fig. 2.—The patient was a 27-year-old man with extensive loss of the coronal portion of the upper lateral incisor due to traumatic injury about eleven months prior to admittance for endodontic treatment. There was slight mobility of the tooth, with a perforating fistulous tract approximating the apex of the lateral incisor. *A*, Prior to treatment; *B*, diagnostic measurement radiograph; *C*, January, 1955, root canal filled with gutta-percha and eucapercha three weeks after treatment was begun; *D*, February, 1956, postoperative radiograph thirteen months after treatment.

Fig. 3.

Fig. 3.—The patient was a 16-year-old boy with carious exposure of the pulp of the upper right lateral incisor. He presented extensive swelling and edema of the upper right quadrant of the face, with partial closure of the right eye. The tooth was opened and permitted to drain for three days prior to sealing in Endo-cide dressing. *A*, Prior to beginning treatment; *B*, diagnostic measurement radiograph; *C*, June, 1955, root canal filled with gutta-percha and eucapercha seventeen days after first appointment; *D*, June, 1956, postoperative radiograph twelve months after completion of treatment.

DISCUSSION

In any problem of this nature, it is most important that careful attention be paid to the possibility of obtaining false negative culture results in the culture broth tests. Such false negative results may come about by inadvertent contamination of the culture medium with residual antiseptal agent still active

Fig. 4.

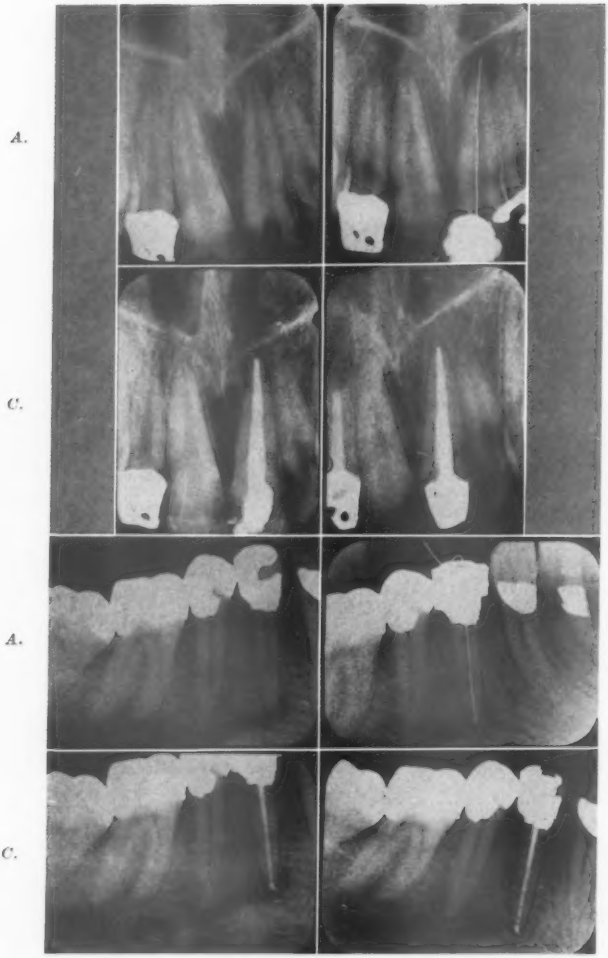

Fig. 5.

Fig. 4.—The patient was a 13-year-old boy with carious exposure of the pulp of the upper right central incisor. The tooth was asymptomatic and slightly mobile. *A*, Prior to beginning treatment; *B*, diagnostic measurement radiograph; *C*, February, 1956, root canal filled with gutta-percha and eucapercha sixteen days after first appointment; *D*, March, 1957, radiograph taken thirteen months after root canal was filled.

Fig. 5.—The patient was a 47-year-old woman with necrosis of the pulp resulting from a deep gingival amalgam filling in the lower left first premolar. There was a perforating fistulous tract approximating the root apex of the first premolar. The patient had noted swelling and drainage in the area about six months prior to beginning endodontic treatment. *A*, Case prior to beginning treatment; *B*, diagnostic measurement radiograph; *C*, February, 1955, root canal filled with gutta-percha and eucapercha seventeen days after first appointment; *D*, April, 1956, postoperative radiograph taken fourteen months after the case was completed.

in the canal. From a previous work, not yet published, and from more recent investigation, we have determined that this factor is at a minimum if the antiseptal dressing remains in the root canal ninety-six hours. Therefore, the patients cooperating in this study were scheduled with appointments separated by intervals of four or more days and usually not exceeding seven days.

Fig. 6.

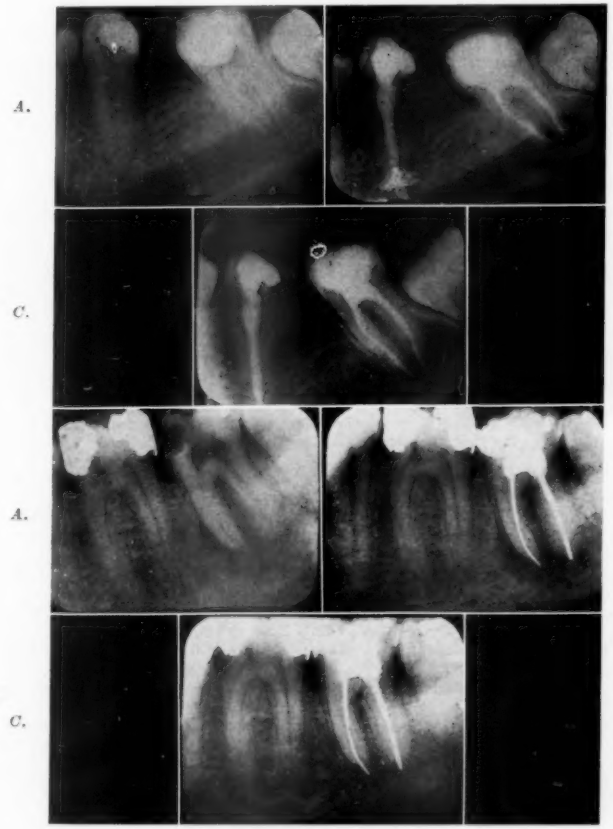

Fig. 7.

Fig. 6.—The patient, a 14-year-old girl, had a history of a partial pulpectomy having been attempted on the lower right second molar. The tooth became sensitive to percussion. Upon removal of filling and capping material, a putrescent odor was noted. *A*, Prior to treatment; *B*, May, 1955, root canals filled with gutta-percha and eucapercha nineteen days after beginning treatment; *C*, January, 1956, postoperative radiograph taken eight months after completion of treatment. No further postoperative radiographs were available.

Fig. 7.—The patient was a 32-year-old man with complete necrosis of pulp resulting from recurrent caries around a mesial amalgam filling. The tooth was extremely mobile. *A*, Case prior to beginning treatment; *B*, January, 1957, case showing root canals filled with silver cones and silver cement twenty-nine days after beginning treatment; *C*, August, 1957, postoperative radiograph taken eight months after case was completed.

A glance at Fig. 1 will show that 90.5 per cent of all cases were treated successfully in four appointments, which was the minimum number of visits for completion of a case under the described clinical testing program, 7.2 per cent

of the cases were completed in five appointments, and 2 per cent required six visits. One case required seven appointments. We consider this performance as extremely successful in that all cases involved pulpless teeth, many of which presented extensive periapical bone involvement and large granulomas. In a similar manner, the rapid regeneration of periapical bone tissue, as shown in Fig. 1, was not only highly satisfactory but indicative, in our opinion, of a marked lack of toxicity of Endo-cide.

No side reactions of any kind were observed in any patients chosen for this study. Careful vigilance was exercised in this respect, since both para-aminotoluene sulfonamide and 5-nitro-2-methylfurfuryl ether contain exposed nitrogen-containing radicals which may cause some unwanted side reactions.

CONCLUSIONS

1. The chemotherapeutic mixture of para-aminotoluene sulfonamide and 5-nitro-2-methylfurfuryl ether, used as described, has proved to be a highly effective bactericidal agent for use in the practice of endodontics.

2. Because of Endo-cide's wide antimicrobial spectrum, lack of toxicity and side reactions, complete ease of use, relative lack of culture problems, and high clinical efficiency, we regard this agent to be clinically superior to previously existing endodontic bactericidal agents.

REFERENCES

1. Sommer, R. F.: Essentials for Successful Root Resection, AM. J. ORTHODONTICS & ORAL SURG. 32: 76, 1946.
2. Endodontic Technique Used at University of Illinois, School of Dentistry.
3. Jasper, E. A.: Essentials in Endodontic Practice, ORAL SURG., ORAL MED. & ORAL PATH. 2: 1199, 1949.
4. Grossman, L. I.: Evaluation of Antibiotic Agents for Root Canal Treatment, New York J. Dent. 15: 232, 1945.
5. Grossman, L. I., and Stewart, G. G.: An Effective Penicillin-Streptomycin Suspension for Endodontic Treatment, ORAL SURG., ORAL MED. & ORAL PATH. 2: 274, 1949.
6. Grossman, L. I.: Polyantibiotic Treatment of Pulpless Teeth, J. Am. Dent. A. 43: 265, 1951.
7. Casey, G. J., Gurney, B. F., and Rapp, G. W.: A New Drug and Its Clinical Application, Bur 47: 108, 1947.
8. Gurney, B. F., Casey, G. J., Carroll, R. J., Restarski, J. S., Best, E. J., and Conlin, A.: Endodontic Therapy With Para-Aminotoluene Sulfonamide Hydrochloride (Benzylog), J. Am. Dent. A. 56: 329, 1958.
9. Gurney, B. F., and Best, E. J.: A New and Superior Endodontic Bactericidal Agent, Part I, ORAL SURG., ORAL MED. & ORAL PATH. 12: 104, 1959.

PHARMACOLOGY AND THERAPEUTICS

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DRUG CONTROL OF THE DENTAL SALIVARY PROBLEM

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INTRODUCTION

DENTAL procedures present enough problems at best without the presence of excess saliva, which reduces accuracy and thoroughness and tends to tire the operator. Saliva can reduce visibility and thus obscure defects from the eyes of the dentist. Accordingly, quality dentistry demands that the operator exert a measure of control over excessive secretions, especially in the case of difficult procedures.

A survey of medical literature[1-6] shows that the medical profession is using drugs to help control the problem of excess secretions. Mechanical aspiration to remove the accumulating secretions fails in many instances to produce a desirable working field. When aspiration is combined with a drug that arrests these secretions temporarily, however, an ideal working field is much easier to obtain.

The use of a preoperative drying agent in the ambulatory dental patient poses certain special problems with which the medical surgeon does not have to contend. Any agent producing sialoschesis or suppression of salivary secretion for routine use in the average dental practice should meet the following requirements:

1. It should produce good reduction of salivation.
2. It should be easy to administer, preferably by mouth.
3. It should be specific enough for excess salivation so that the patient can be ambulatory within an hour or two, unhampered by undesirable side effects.
4. It should be compatible with other routine dental agents, such as anesthetics, hypnotics, and antibiotics.

HISTORY

Medical anesthesiologists have narrowed the choice of drugs suppressing the flow of saliva that would fit these criteria. All that have been proved to be of value have fallen into the group that pharmacology books list as anticholinergic drugs.

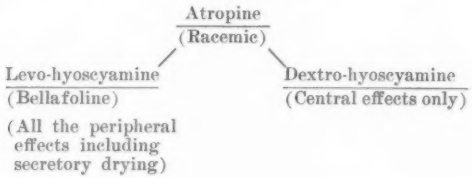
Leigh and Belton[4] found scopolamine superior to atropine in decreasing secretions. Milani and Artola[1] found that levo-hyoscyamine afforded satisfactory inhibition of secretions preoperatively in 85 per cent of a group of children as compared with only 41 per cent effectiveness for atropine. Griggs, Adriani, and Berson[2] evaluated levo-hyoscyamine, scopolamine, atropine, Banthine, and Demerol for use in throat operations in children. Atropine "proved to be quite disappointing." Demerol also proved to be poor. Banthine arrested salivation well, but the side effects of hyperthermia and tachycardia were excessive. Only levo-hyoscyamine and scopolamine proved satisfactory, both ranking about the same. In a later study, Griggs and Adriani[3] found that scopolamine does not protect the heart against vagal stimulation, whereas levo-hyoscyamine does. Wise, Tillman, and Crawford,[6] using levo-hyoscyamine subcutaneously in children as a preoperative drying agent, report that it is somewhat faster in action than scopolamine. They also found the slight central sedative effect of levo-hyoscyamine more desire than the occasional disorientation and hallucinations that are reported with scopolamine. No discernible respiratory depression or hyperthermia was noted with levo-hyoscyamine.

It should be noted from these reports that the incidence and degree of side effects played a major role in the assessment of the usefulness of these drugs. Dentistry should go even further than medical anesthesiology in avoiding undesirable side effects in ambulatory patients, since good toleration increases the clinical value of such an agent.

These specific reports on the effectiveness of levo-hyoscyamine (Bellafoline, a product of Sandoz Pharmaceuticals, Hanover, New Jersey) to arrest salivation, plus other reports of its efficacy in controlling spasm,[7-12] led us to conclude that it would be a logical agent with which to premedicate dental patients for salivary suppression.

PHARMACOLOGY

Bellafoline comprises all the levorotatory alkaloids of belladonna, principally levo-hyoscyamine. Goodman and Gilman,[13] Cushny,[14] and authors of other standard pharmacology texts point out that it is this levorotatory form of belladonna that is therapeutically active. For example, Goodman and Gilman[13] say: "Atropine is racemic, being a mixture of equal parts of the optical isomers of hyoscyamine. Inasmuch as dextro-hyoscyamine has weak peripheral actions in the body, atropine owes its potency chiefly to its content of levo-hyoscyamine. The latter has the same central actions as atropine but is twice as powerful in its peripheral autonomic effects."



METHOD OF APPLICATION

I well appreciate the limitations of subjective analysis in comparison to controlled studies. However, proof of levo-hyoscyamine's value as an antisialagogue has already been established. The purpose of this study was to evaluate the clinical effect of this drug on the dental patient and to see whether it met the previously established criteria for a dental antisialagogue. The best controlled studies must also be proved by careful clinical observation during everyday practice under a variety of conditions.

Studies on levo-hyoscyamine as a dental drying agent have been made over a period of two years of active dental practice. Over 1,500 doses have been administered during this time, with notes kept on degree of salivation (estimated as light, medium, or heavy), body type (whether small, medium, or large), and time lapse from the administration of levo-hyoscyamine to the point where the operator no longer noticed a moisture problem.

Where indicated, Nembutal was employed to alleviate central excitation and to potentiate anticholinergic (including drying) effect. The dosage of Nembutal varied from 0.75 grain in mildly excited persons to 1.5 grains in highly nervous patients.

Most patients in this study were premedicated, as described, for periodontal surgical procedures or other related operations. In many instances a local anesthetic was also employed.

Also evaluated was Elixir Belladenal, which is a liquid form of levo-hyoscyamine (Bellafoline) and phenobarbital. The results with this form were good, but it is felt that phenobarbital's onset of action is too slow and its duration of effect is too long for the average dental procedure. It is preferable to use a short- or medium-acting barbiturate.

RESULTS

It was noted, as one would suspect, that larger body types usually needed more drug than smaller body types. Otherwise, the main factor that determined dosage of levo-hyoscyamine was the degree of salivation. Table I shows the amount of levo-hyoscyamine found to be appropriate for three types of salivators. We employed tablets, each containing 0.25 mg. levo-hyoscyamine.

TABLE I

DEGREE OF SALIVATION (VISUALLY ESTIMATED)	AMOUNT OF LEVO-HYOSCYAMINE AND TIME OF ADMINISTRATION
Light	1 tablet 1 hour before operation
Medium	2 tablets 1 hour before appointment
Heavy	1 tablet 4 to 6 hours before appointment time, followed by 2 tablets 1 hour before appointment

The tablet may be ingested orally, or it may be absorbed sublingually if a more rapid effect is desired. Since the tablet is tasteless and easily disintegrated, the patient does not object to this latter method of application.

TABLE II

GOOD (PER CENT)	FAIR (PER CENT)	POOR (PER CENT)
70	20	10

Good indicates adequate reduction of salivary flow to produce a desirable operative field.

Fair indicates a slight reduction but a somewhat noticeable salivary flow still present.

Poor indicates no reduction in salivary flow noted.

Using the above dosage schedule, there were no noticeable side effects that could be attributed to levo-hyoscyamine alone. Slight variation in the duration of action of levo-hyoscyamine was observed. It should be noted that any drug containing belladonna is contraindicated in severe cases of glaucoma.

Our estimate of the degree of effectiveness of this drug can be seen in Table II.

The percentage of effectiveness does not totally reflect the efficiency of the drug itself, since there is a likelihood of human error in judgment in the dosage selected for each patient. In other words, it is entirely possible that an additional half tablet would have converted a fair result to a good result. A measure of control was afforded by those instances in which levo-hyoscyamine was not employed. For example, for a surgical procedure the individual patient received the described medication, but the drug was withheld on some subsequent related appointments. The abundant salivary flow observed in the latter instances increased our awareness of the helpful effects of the drug.

DISCUSSION

There is no phase of dentistry that is not benefited by salivary control. The reader can no doubt think of many instances in which such control would prove advantageous.

With good observation of the degree of salivation and with proper dosage, the results of salivary control with levo-hyoscyamine are considered to be predictable within reasonable limits.

It is encouraging to find a drug which will meet the previously laid down criteria for an antisialagogue. The antispasmodic action of the drug also seemed to be helpful, especially in curbing the nausea experienced by some patients. In addition, the "gag reflex syndrome" seemed to be controlled in several typical gagging patients. This latter observation is one that bears further investigation and confirmation, since it would add immeasurably to the value of this agent.

CONCLUSION

1. The need to bring salivation under the control of the dental operator is recognized.

2. A review of secretion-suppressing drugs from the field of medical anesthesiology is presented.

3. A drug, levo-hyoscyamine, was tested clinically to determine its usefulness as a dental antisialagogue. It was found to satisfy the following requirements:

(a) It is a good salivary inhibitor.

(b) It is easy to administer.

(c) It gives no discernible clinical side effects.

(d) It is not contraindicated in the presence of other routine dental drugs commonly employed.

REFERENCES

1. Milani, R. E., and Artola, R.: Third Congreso de Anestesiologia, 1951, p. 251.
2. Griggs, T., Adriani, J., and Berson, W.: Aids to Pediatric Anesthesia, Anesth. & Analg. **32**: 340, 1953.
3. Griggs, T. S., and Adriani, J.: Some Advances in Pediatric Anesthesia, South. M. J. **47**: 323, 1954.
4. Leigh, M. D., and Belton, M. K.: Premedication in Infants and Children, Anesthesiology **7**: 611, 1946.
5. West, J. S., and Papper, E. M.: Preanesthetic Medication for Children, Anesthesiology **11**: 279, 1950.
6. Wise, G. F., Tillman, W. W., Jr., and Crawford, O. B.: Premedication for Operative Procedures; Fundamental Considerations in Selection, Missouri Med. **51**: 914, 1954.
7. Kramer, P., and Ingelfinger, F. J.: Use of Antispasmodics and Spasmodics in Treatment of Gastrointestinal Disorders, M. Clin. North America **32**: 1227, 1948.
8. Beakey, J. F., Bresnick, E., Levinson, L., and Segal, M. S.: Evaluation of Therapeutic Substances Employed for Relief of Bronchospasm; Anticholinergic Agents, Ann. Allergy **7**: 113, 1949.
9. Bargen, J. A.: Psychosomatic Aspects of Digestive Disorders, Gastroenterology **13**: 604, 1949.
10. Bargen, J. A.: The Problem of the Syndrome of the Irritable Bowel, Gastroenterology **30**: 703, 1956.
11. Miskimon, R. M.: Report of 700 Cases of Irritable Colon in Private Practice, Virginia M. Month. **81**: 109, 1954.
12. Hardin, J. H., Levy, J. S., and Seager, L.: Clinical Comparison of Antispasmodic Drugs, South M. J. **47**: 1190, 1954.
13. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, 1940, The Macmillan Company, p. 462.
14. Cushny, A. R.: Pharmacology and Therapeutics, ed. 12, Philadelphia, 1940, Lea & Febiger, p. 502.

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ARMED FORCES AND PUBLIC HEALTH SERVICE

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METHODS USED IN EVALUATION OF HIGH-SPEED DENTAL INSTRUMENTS AND SOME RESULTS

Joseph L. Bernier, Colonel, DC, USA, and Milton J. Knapp, Captain, DC, USA

INTRODUCTION

DURING a recent two-year period, the Dental and Oral Pathology Branch at the Armed Forces Institute of Pathology tested and compared fourteen high-speed dental instruments. The primary aim was to determine whether or not the important gains in cutting efficiency might be outweighed by deleterious effects of high speed on patients, operators, or teeth. It was also expected that one of the instruments might be recommended for use by the Army Dental Corps. This was not done for several reasons, including the fact that marked improvements were made in some instruments so near the end of our test period that they could not be included for evaluation.

It is the purpose of this article to present the methods used in evaluation as well as some results of our experience with the high-speed cutting devices. Two aspects are discussed in detail, namely, (1) the biologic effects of high-speed instrumentation on the dental pulp and (2) the possible acoustic trauma to the operator through continued exposure to sounds of the intensity inherent in high-speed instrumentation.

METHODS OF RATING

The methods adopted for comparisons of our fourteen instruments are presented both as a possible guide to members of the profession who may be engaged in similar tests and as a basis for discussion of considerations found to be important in selection of any high-speed dental instrument.

Selection of Factors for Rating.—An attempt was made to compare the instruments as objectively as possible. All possible factors obtained through our observation and testing period were listed, and statistical advice was

obtained as to those which would achieve maximum objectivity. The rating elements finally selected comprised four main categories—instrument efficiency, effects on patient, effects on operator, and miscellaneous aspects. The twenty-one rating elements in these categories and the definitions of each are shown in Table I.

TABLE I. RATING ELEMENTS AND DEFINITIONS

CATEGORY	RATING CATEGORY AND ELEMENTS	DEFINITIONS
A.	Instrument Efficiency	
	1. Power transmission	1. Power transmission from source to bur; rated on maneuverability
	2. Cutting efficiency	2. Highest rating assigned to speeds of 100,000 r.p.m. or over, on basis of Kilpatrick's[3] work
	3. Speed control	3. Rated on variability
	4. Torque	4. Based on amount of force needed to push a tooth into a revolving bur in order to stall bur
	5. Bur reversibility	5. Reversible or not reversible
	6. Chuck efficiency	6. Based on test drilling; measurement of corrected diameter of bur against drilled hole
	7. Cooling systems	7. Based on combinations of air and water, with and without selectivity
B.	Effects on Patient	
	1. Noise level	1. Decibel level directly proportional to irritational effect at 76 decibels and above
	2. Cutting efficiency	2. Patient comfort based on relative speed of instrument, which reflects cutting efficiency
	3. Safety in torque (soft tissue)	3. The less the torque, the greater the safeguard to soft tissue
	4. Safety in torque (cavity preparation)	4. The greater the torque, the more the tactile sensation and consequently less danger of pulpal exposure
C.	Effects on Operator	
	1. Hazard from noise	1. Highest decibel level 76 and over rated as most likely to produce acoustic trauma
	2. Fatigue from working pressure	2. Optimum torque range set at 10 to 30 oz. pressure; above 30 oz. considered physically tiring; below 10 oz. considered mentally tiring
	3. Fatigue based on unwieldiness of handpiece	3. Rated on 5 factors: spray attachment, position at which tubes enter handpiece, over-all size, size of operating head, and length of handpiece
	4. Facility of foot control	4. Based on design of foot control
	5. Fatigue from handpiece weight	5. Based on actual weights of handpiece, in grams
D.	Miscellaneous Aspects	
	1. Range of operative procedures	1. Based on facility of cutting various preparations and other operations, such as prophylaxis and polishing
	2. Tractability of handpiece design	2. Smoothness of handpiece design
	3. Chuck durability	3. Estimate of length of life
	4. Ease of cleaning	4. Based on estimate of time per hour of use for cleaning, lubricating, and sterilizing under ordinary operating conditions
	5. Acceptability of sterilization techniques	5. Based on method of sterilization

Testing Devices.—Two special testing devices were required to obtain information on which to base comparative ratings. These are briefly described and the measurement techniques are explained in the following paragraphs.

A special test was required to measure the *efficiency of the chucks.* The apparatus for drilling the centric holes consisted of a machined aluminum jig and chucking device that would hold any dental handpiece. Two precisely machined metal blocks—one small and the other larger—were placed underneath, and the handpiece was adjusted so that the bur could be placed in flat horizontal alignment against the lower block. The upper block, which was machined so that it was perpendicular to the lower block, was used for lateral alignment of the bur. A strip was mounted at right angles to the base of the jig. A small ivorine block was then pushed along the guide strip into the revolving bur in a direction parallel to the axis of the bur. The hole produced was measured with a micrometer on a microscope.

Nomographs were constructed for graphic computation of relative variations between bur size and drilled hole. Chart 1 shows an example of how such a nomograph might be utilized. In making the desired computations, the first step is to find the true bur diameter* on the left-hand scale. Next, the diameter of the hole (that was drilled with the same bur) is located on the center scale. Finally, a line is drawn to pass from the first point *through* the second point until the right-hand scale has been intercepted; the value of the intercept is the per cent variation for the chuck which held the bur. This is predicated on the hypothesis that if the chuck had no wobble or eccentricity, the diameter of the hole would closely approximate the true diameter of the bur; therefore, the difference between bur diameter and hole diameter is largely due to the eccentric rotation of the chuck. The per cent variation is this difference as a percentage of the true bur diameter. The closer this value comes to zero, the more efficient is the chuck.

Chart 1 permits direct comparison of one type of drive with another. The most efficient chuck from each type has been selected for this purpose. The nomograph values are taken from four basic charts, one for each type of instrument.

The linear speed of the cutting tool, determined by its diameter, governs the rate of energy applied to remove the tooth structure. Kilpatrick[1, 2] points out that with the higher rotational speeds better preparations can be completed more rapidly and with reduced vibration, resulting in less tension for patient and operator. On the basis of his work, speeds of 100,000 r.p.m. and over produce maximum cutting efficiency. Speeds in the range of 100,000 r.p.m. and over were obtained with all three of the belt-driven handpieces and the air turbines.

In combination with the r.p.m., the energy developed by the driving mechanism determines the efficiency of a dental instrument. This energy is called *torque* and in our tests was measured by the amount of pressure required to stall a revolving bur while cutting tooth structure.

The apparatus used for measuring the torque of the fourteen instruments consisted essentially of a closed air pressure system which was connected to

*True bur diameter means the actual diameter of the bur plus the bur's own eccentricity.

a large Luer-Lok syringe. A jig for holding the tooth was then mounted on the plunger. The plunger with the mounted tooth was forced against the revolving bur by air pressure. The pressure at the point at which the bur stalled, with the instrument operating at maximum speed, was defined as the amount of torque.

On the basis of these tests, the torque of all gear- and belt-driven handpieces amounted to 56 ounces or more. The lowest torque rating was 6 ounces for each of two air turbines.

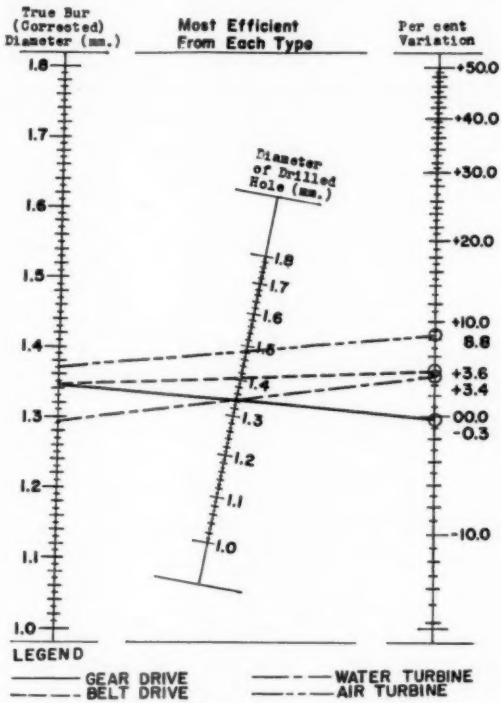


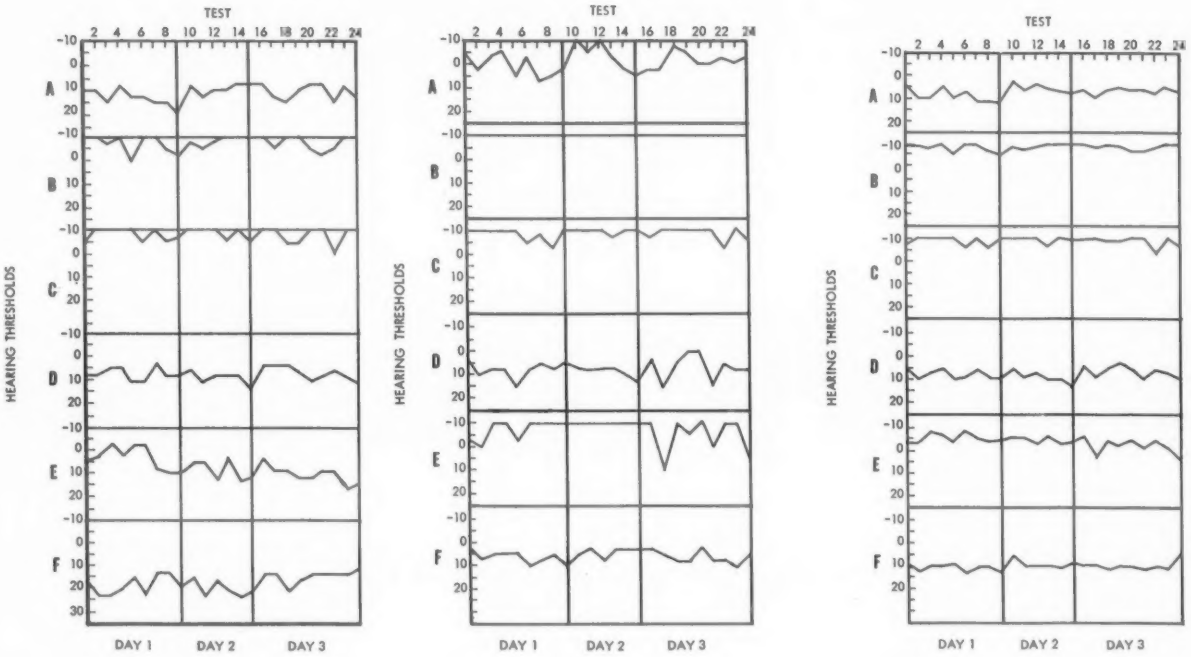
Chart 1.—Relative efficiency of chucks.

A major problem arising from introduction of high-speed dental instruments is that of possible acoustic trauma to the operator through continued exposure to sounds of the intensity inherent in such speeds. In recognition of this danger, *a human exposure experiment* was conducted. The verbatim report follows:

Operator Hazard Sound Experiment

(Report of the Bioacoustic Laboratory of the Audiology and Speech Center on the Variations in Human Thresholds of Hearing Following Exposure to a Representative Air Turbine Dental Drill)

"As a portion of the multifaceted evaluation of air turbine dental drills, the following hypothesis was examined: If human beings are exposed to



A. *B.* *C.*

Chart 2.—*A*, Thresholds at 6,000 c.p.s. averaged for left and right ears. *B*, Thresholds for each subject at 8,000 c.p.s. averaged for left and right ears. *C*, Thresholds for each subject, averaged over 4,000 c.p.s., 6,000 c.p.s., and 8,000 c.p.s. frequencies, and left and right ears.

Test 1 represents pre-exposure test. Letter designations refer to subjects tested.

sounds of this intensity, there will be no essential change in their threshold of hearing.

"*Subjects:* Six subjects, all members of the dental staff of the Armed Forces Institute of Pathology, participated in the study.

"*Procedure:* Subjects were tested in a pre-dichotomized distended Latin Square to minimize the error introduced by testing each person at the same interval after exposure. All subjects were tested prior to noise exposure. They were then split into two groups of three. Group 1 exposed themselves beginning on the hour and continuing until seven minutes after the hour for each of eight consecutive hours. Group 2 began at fifteen minutes past the hour and underwent the same condition as Group 1. During exposure, the noise was randomly interrupted to simulate actual working conditions. The entire procedure was repeated on each of the three consecutive days, except that on the second and third days the exposure interval was extended to fifteen minutes. Audiograms were taken by two trained audiologists, using standard audiometric procedures, except that frequencies were presented in a partially randomized order. During the experiment an otological examination was given to serve as an additional control on extraneous factors entering the data, and to prevent any auditory mishap.

"Throughout the experiment, any subject showing a threshold shift of greater than fifteen decibels at any frequency was subjected to a test of recovery at that frequency. If, within fifty-five minutes, hearing had not returned to within ten decibels of the initial audiogram, this subject would be dropped from the experiment.

"*Results:* The data were examined as follows: the individual thresholds for each frequency in each test were inspected for the pressure of threshold shift which had been defined as a fifteen decibel change in hearing acuity; thresholds were averaged across ears and across individuals for each frequency and subjected to t-tests; the 4,000, 6,000, and 8,000 c.p.s. averages were pooled and subjected to t-tests. No 't' value for any frequency, or any point in time after the beginning of exposure, was significant at any level. It was also noted that, given homogeneity of variance, no increase in sample size would produce significance. However, it was noted that individual thresholds did not remain constant. They varied (randomly) within plus and minus ten decibels of the initial audiogram. Even though no statistic will recognize these variations, it is within the realm of possibility that these changes are actual clinical entities. With this thought in mind this laboratory urges that further research be undertaken to determine the amount of danger to the hearing mechanism present in these machines."

Chart 2, *A* shows thresholds for each subject at 6,000 cycles per second (c.p.s.), averaged for left and right ears. (*Note:* Test 1 is the pre-exposure test; Tests 9 and 15 on the abscissa scale are the first tests on the second and third days, respectively.) Chart 2, *B* shows thresholds for each subject at 8,000 c.p.s. averaged for left and right ears. Chart 2, *C* shows thresholds for each subject averaged over the 4,000 c.p.s., 6,000 c.p.s., and 8,000 c.p.s. frequencies, and left and right ears.

Noise levels in excess of 75 decibels in frequency ranges of 1,000 to 8,000 c.p.s. may possibly cause acoustic trauma. The extent of the trauma, if any, would depend on the frequency and length of exposure time. All of the instruments in this study were subjected to a frequency band analysis as well as an ambient noise level reading.

Rating Methods.—As previously mentioned, an attempt was made to compare the fourteen high-speed instruments objectively, although it was recognized that there was some element of subjectivity in certain factors to be rated. The statisticians who were consulted designed a basic rating card for this purpose (Chart 3), established strict criteria for each of the twenty-one rating elements to be considered (Table I), and allocated one card to each element. The card permitted direct comparison of each instrument with each of the others and also permitted scoring of the relative position of all the instruments with respect to the individual factor rated.

FACTOR: RELATIVE EFFICIENCY OF CHUCKS

PERCENT VARIATION 100 (HOLE DIA. − TRUE BUR DIA.) −100

L	MACHINE (%)	2	3	4	5	6	7	8	9	10	11	12	13	14	RATING
1	(7.4)	-	-	-	-	+	-	+	-	+	+	+	+	+	7
2	(-0.3)	+	+	+	+	+	+	+	+	+	+	+	+	+	13
3	(-4.4)	-	-	-	+	-	+	-	+	+	+	+	+	+	8
4	(-2.1)	+	+	+	+	+	+	+	+	+	+	+	+	+	12
5	(-4.3)	+	+	-	+	-	+	-	+	+	+	+	+	+	9
6	(-32.6)	-	-	-	-	-	-	-	-	-	-	-	-	-	0
7	(-3.4)	+	+	+	+	+	+	+	+	+	+	+	+	+	11
8	(-17.3)	+	+	+	+	+	+	-	+	+	+	+	+	-	5
9	(3.6)	+	+	+	+	+	+	+	+	+	+	+	+	+	10
10	(21.8)	+	+	+	+	+	+	+	+	+	+	-	-	-	3
11	(-26.3)	+	+	+	+	+	+	+	+	+	+	+	-	-	2
12	(-26.3)	+	+	+	+	+	+	+	+	+	+	+	-	-	1
13	(-21.2)	+	+	+	+	+	+	+	+	+	+	+	+	-	4
14	(-8.8)	+	+	+	+	+	+	+	+	+	+	+	+	+	6

TO RATE, ADD MINUS SIGNS DOWN TO PLUS SIGNS ACROSS FOR COLUMN AND LINE HAVING THE SAME NUMBER.

Chart 3.—Basic rating card.

Two members of the staff of the Dental and Oral Pathology Branch (J. L. B. and M. J. K.) rated each factor, designating by a plus sign that the rated instrument was more satisfactory (better) than the instrument with which it was compared, a minus sign if "worse than," and a zero if there was no difference in the two with respect to the particular factor under consideration. As the sample card indicates, addition of the plus marks in line 1 provided the rank score of the first instrument. (For example, the machine listed on line 1 ranked as instrument No. 7 among the fourteen instruments with respect to chuck

efficiency.) Score ranks of the instruments on successive lines were obtained by adding minus signs down each comparison column to plus signs across the appropriate rating line.

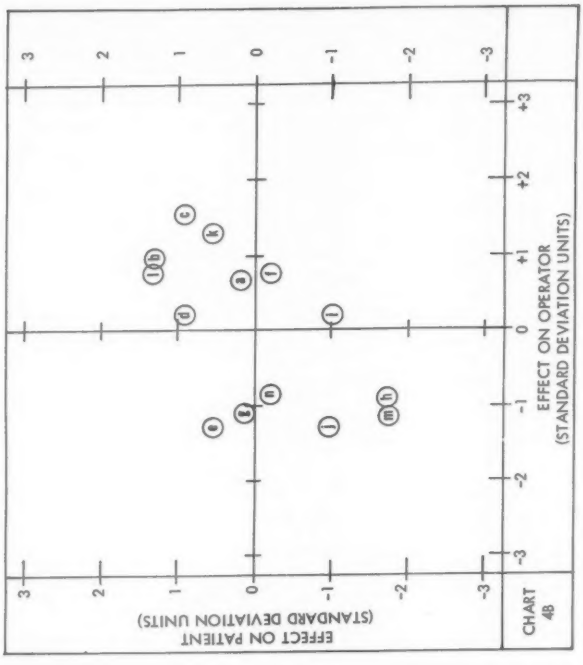
When all the instruments had been rated, the basic rating cards for each element were handed to the staff of the Medical Statistics Section for checking and for score evaluation. Since the major purpose of the scoring was to recommend one or more instruments to the Army Dental Corps, consideration of initial costs and interchangeability of stones and burs with those of conventional low-speed instruments was necessary. For this reason, the instruments were first compared within types, that is, gear-driven, belt-driven, water turbines, and air turbines. This comparison is reflected in the chuck efficiency nomograph (Chart 1).

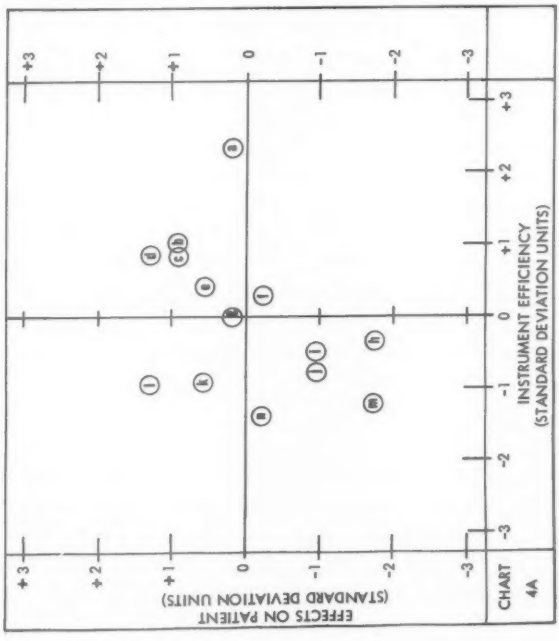
No composite scores were attempted since some elements were rated more than once (for example, noise level as an operator hazard and as a factor irritational to the patient). However, an association of the individual scores for patient effects, operator effects, and the miscellaneous elements were related successively to the efficiency of each instrument by translating the scores for each category into standard scores[4] to reflect the instrument-dispersion relative to the category mean. These relationships are presented in Chart 4, *A* through *C*; Chart 4, *D* relates the effects of the instruments on patients to those on operators. Instruments which appear in the upper right quadrant of the charts are above average in both categories under consideration; those in the upper left quadrant are above average for the category measured on the vertical scale and below average for that on the horizontal scale. Instruments shown in the lower right quadrant are the converse of those in the upper left, while those in the lower left are below average for both categories.

The four parts of Chart 4 indicate that, in general, the instruments with elements that contributed most to efficiency also had "plus" elements in relation to patients and operator effects. The converse was also true. It is of particular interest that when the scores for rating category 2 ("Effects on Patient") were related to effects on operator (Chart 4, *B*), six of the fourteen instruments rated very high in both categories. The association of miscellaneous aspects and instrument efficiency in Chart 4, *C* serves to penalize some instruments which rated high in other categories; only two of the instruments appeared in the upper right quadrants of all four charts. Recent improvements of several instruments would undoubtedly increase the number with consistently high ratings if similar tests were made.

PULPAL CHANGES

Perhaps the most important consideration in the use of high-speed instruments is the biologic effects on the dental pulp. Both animal and human experimentation were undertaken, and considerable data were accumulated. These data must be evaluated in the light of certain established facts concerning the capacity of the dental pulp to react.





(*For legend, see opposite page.*)

Chart 4.—*A*, Effects on patient related to instrument efficiency in terms of standard scores. *B*, Effect on patient related to effect on operator in terms of standard scores. *C*, Miscellaneous aspects related to instrument efficiency in terms of standard scores. *D*, Effects on operator related to instrument efficiency in terms of standard scores.

Status of the Clinically Normal Pulp.—The pulp is accepted as "clinically normal" when it exhibits neither signs nor symptoms and when it responds as expected to certain accepted testing procedures. In view of the questionable validity of such tests, the results may not always be meaningful. We must assume, therefore, that the health status of the dental pulp is variable and that extensive pathologic changes, such as calcific degeneration and even pulpal abscesses, may exist without detection. Histologic examination of thousands of extracted teeth has shown this to be true. Because of this, reactivity of the dental pulp to any stimulus will depend largely on the remaining threshold of defense. If this fact is not recognized and properly weighed in investigative procedures, serious errors in conclusions will result.

Reactivity of the Clinically Normal Pulp.—Of equal importance is the need for recognizing that the dental pulp is an extremely sensitive organ with surprising powers of recovery. *Any operative procedure, even hand instrumentation, will result in a tissue reaction within the pulp.* In most instances, such a reaction will not produce symptoms, and considerable time may be required for recovery. As in other sensitive tissues, all such events exact their toll, lowering the remaining threshold of the capacity of the pulp for repair. It must also be pointed out that, with aging, catabolic changes are greatly accelerated, and the adult pulp histologically and clinically is quite unlike that of younger persons.

Changes in the Pulp and Dentine With Low-Speed Instrumentation.—Numerous studies have indicated that the pulpal changes brought about by use of the conventional low-speed instruments can be referred to as follows:

1. The calciotraumatic response is a persistent linear marking in the dentinal tubules brought about by a momentary interference with dentine formation at the cavity base at the time of the trauma. In itself, it is not particularly important, since in most instances normal dentine formation is resumed upon cessation of the insult.

2. Disruption in the odontoblastic layer may result from instrumentation of any speed; normally, the columnar odontoblasts are sharply regimented as they engage in dentine formation, but the impact of cavity preparation disrupts their alignment and therefore their function, thus altering the quantity and quality of their product (dentine). This aberration is subsequently seen in the older dentine as the calciotraumatic response. If one recalls that dentine formation is continuous, this can be easily visualized (Fig. 1).

3. Pulpal inflammation, which occurs in areas of the pulp adjacent to the base of the cavity, is of prime importance, since it underlies the changes described above. The severity of this inflammatory change depends upon the nature and intensity of the insult. Usually it is a fairly mild, acute exudative response, characterized by a sparse leukocytic infiltration accompanied by vascular distention and plasma exudation. With time, the cellular infiltrate changes to a lymphocytic

and plasma-cell type. On occasion, however, the traumatic event may produce rupture of blood vessels with escape of whole blood into the pulpal tissue (Fig. 2).

The nature and severity of the inflammatory response determine the extent to which the metabolic activity of the odontoblasts will be disrupted; therefore, they are the chief factors in bringing about the

Fig. 1.

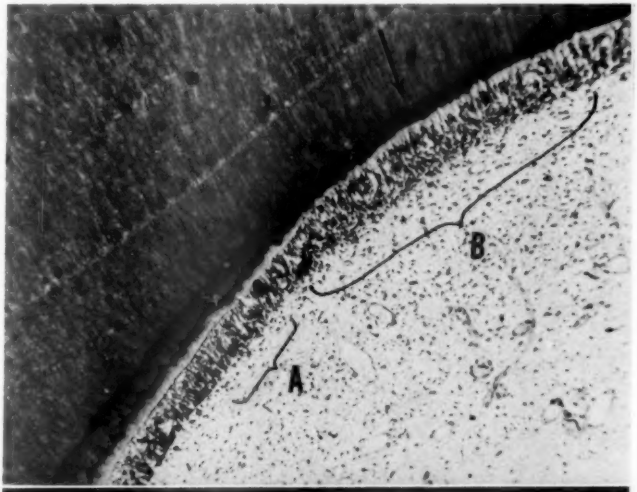


Fig. 2.

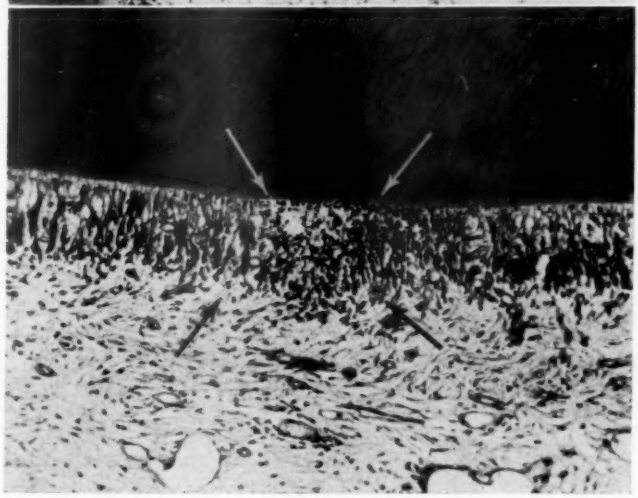


Fig. 1.—Area *A* beyond confines of cavity preparation shows well-oriented odontoblastic layer. Area *B* beneath the cavity preparation exhibits complete architectural disruption. The calciotraumatic response is seen below the arrow.

Fig. 2.—Extravascular hemorrhage in the odontoblastic zone and surrounding tissue.

calciotraumatic response. Even though many changes may have taken place in the pulp, it is seldom destroyed by cavity preparation. Nevertheless, it is certainly possible that it could be, particularly when the additive effect of filling materials on the pulp is significant.

Changes in Pulp and Dentine due to High-Speed Instrumentation.—Experimental procedures were conducted on teeth of dogs and human beings to determine what changes were attributable to high-speed instrumentation.

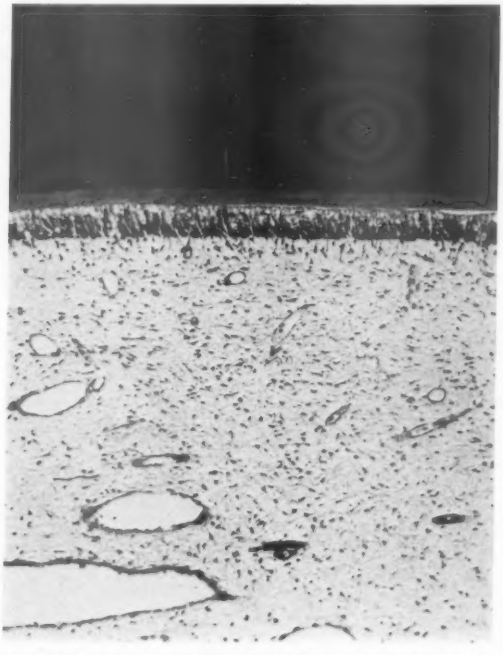


Fig. 3.—Normal histologic appearance of dentine, odontoblastic zone, and pulp.

Experiments: To obtain teeth of reasonably standard size and free of general or local disease, young adult purebred beagle dogs were chosen for the experiments (Fig. 3). Class V cavities were prepared by as standardized a procedure as possible, leaving 1 mm. of dentine between the floor of the cavity and the pulp. Water spray coolant was used during the procedures. The cavities were filled with silver amalgam, without base or cavity lining. Dogs were sacrificed after two, seven, ten, fifteen, and thirty days. The jaws were cut into blocks, decalcified, embedded in celloidin, and cut and stained in the usual manner. Intact contralateral teeth served as controls.

In the human studies, virgin upper and lower premolars, destined for extraction because of orthodontic measures, were used. Cavities were prepared and the teeth were removed after ten and twenty days. They were processed in the usual manner.

Results: Only those changes which are considered to be significantly related to high-speed instrumentation will be discussed. These are (1) rebound response and (2) varicosity.

Rebound response is a change in the dental pulp never before described. The selection of this term to define the reaction in no way implies a factor of causation. Of particular significance is its location on the wall of the pulp chamber opposite, or at least at a distance from, the cavity preparation. While the biologic nature of the change is not yet clear, it appears to be a disturbance in the interstitial ground substance. No cellular infiltrate is noted, and vascular alterations are absent (Figs. 4, 5, and 6).

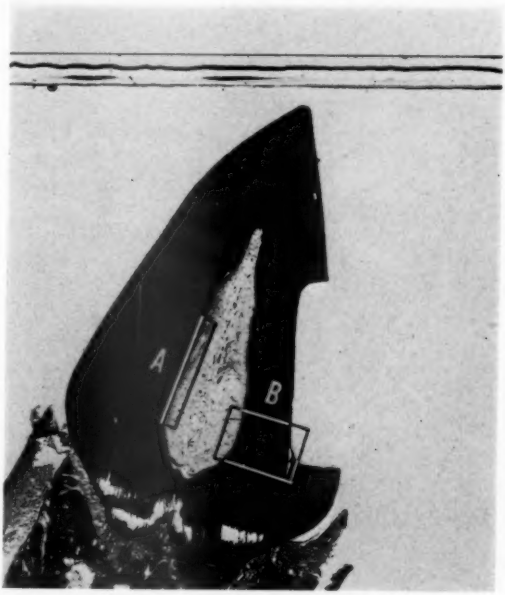


Fig. 4.—Cavity preparation and area of rebound response.

It could be reasoned that with high-speed instruments there is an extensive transmission of energy into the pulp chamber which transcends those forces that would normally localize such effects at the base of the cavity. One could also assume that the physical characteristics of the chamber might influence the point of localization. The change has been seen in both animal and human teeth and will be explored further. An assessment of the cyclic quality of the sound vibrations peculiar to high-speed instruments seems a likely place to begin, in that the rebound response seems similar, at least histologically, to that in teeth subjected to ultrasonic vibrations (29,000 cycles per second).

Fig. 5.

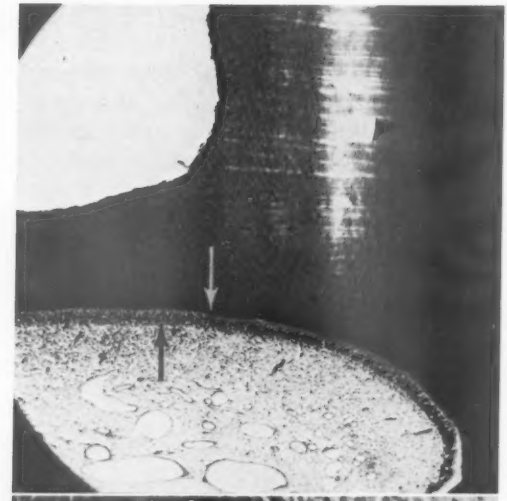


Fig. 6.

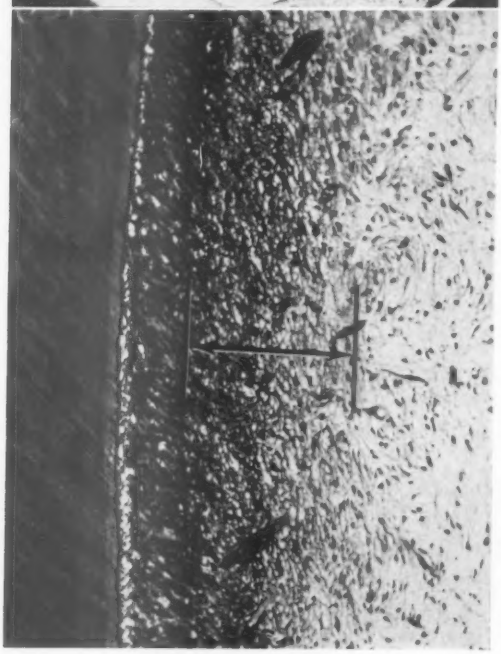


Fig. 5.—Area *B* of Fig. 4. Note calciotraumatic response and disrupted odontoblastic zone.

Fig. 6.—Rebound response of area *B*, Fig. 4.

Varicosity, the second unusual reaction noted in the experimental teeth, was the formation of large air-filled spaces in the pulpal tissue. These were devoid of any lining cells, suggesting that the response was immediate (Fig. 7). As in the rebound response, there are at least speculative reasons which would indicate that energy transmission and focalization could be responsible. If this were so, there is the possibility that some tissue resistance was encountered which precluded the localization of the reaction across the pulp from the site of cavity preparation. One need hardly emphasize the importance of this change in relation to pulpal pain at increased altitudes.

Fig. 7.—Varicosity formation.

Other responses related to high-speed instrumentation include increased odontoblastic disruption, extravascular hemorrhage, predentine formation, and pulpal fibrosis (Figs. 8, 9, 10, and 11). We cannot, however, evaluate the accentuation of these reactions critically on the basis of present studies. Further investigation is required.

Comment: It appears that high-speed instrumentation produces a greater range of pulpal changes, and some may be more severe than the changes produced with low-speed devices. The nature of these changes indicates that their additive effects, if superimposed on a lowered threshold of adaptability of the pulp, could cause irreversible damage.

Fig. 8.

Fig. 9.

Fig. 8.—Odontoblastic disruption.
Fig. 9.—Cells in dentinal tubules.

Fig. 10.

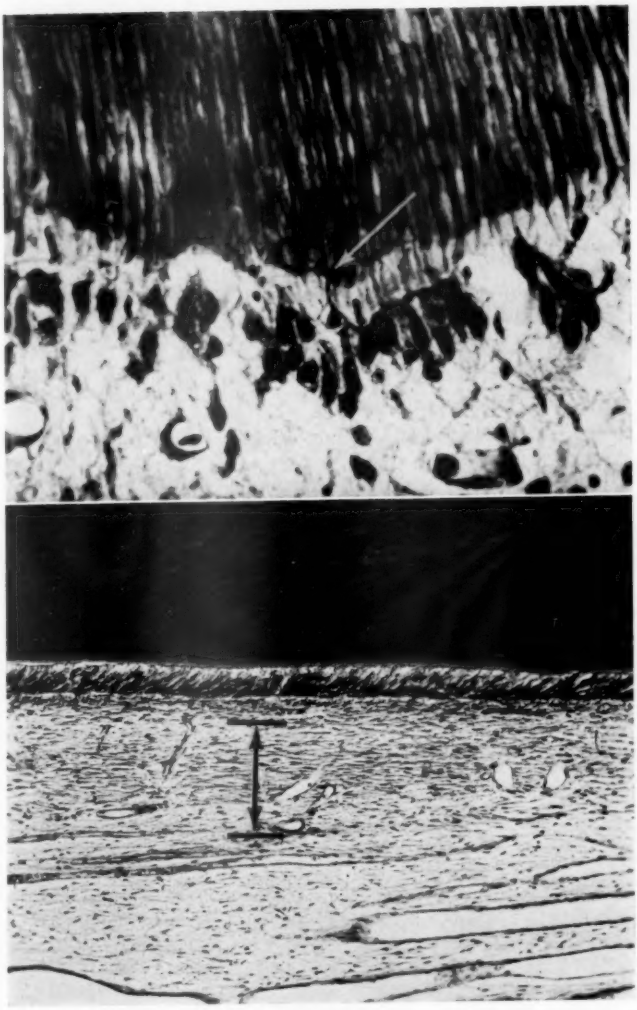


Fig. 11.

Fig. 10.—Aspirated odontoblast.
Fig. 11.—Pulpal fibrosis.

Our inability to relate this range of tissue reactions to specific instruments or speed ranges suggests that the method and the care taken by the operator in using high-speed instruments may be important factors. It is reasonable to assume that experience gained over the years with low-speed instruments may require re-evaluation when applied to the high-speed devices. There is good reason to believe that it is the operator using high-speed instruments as he would the low-speed ones who is responsible for the greater range of pulpal reactions. We believe that studies are indicated to determine how the operator can prevent excessive pulpal damage by controlling the energy of the intensity produced by high r.p.m. instruments. It may be that the lower torque of air turbines will prove to be a factor of safety.

SUMMARY

Methods used in evaluation of high-speed dental instruments at the Armed Forces Institute of Pathology during a two-year period are presented as possible guides for future tests. These include the methods and results of a human sound experiment to determine the effects of high-speed instruments on thresholds of hearing.

The biologic effects of high speeds on the dental pulp were investigated by means of both animal and human experiments; the pulpal changes are discussed and microphotographs are presented.

The views expressed in this article are those of the authors and do not necessarily represent the views of the Armed Forces Institute of Pathology and the Department of the Army.

REFERENCES

1. Kilpatrick, C.: Trauma Reduction in Cavity Preparations Utilizing Rotational Speeds in Excess of 60,000 R.P.M., D. Digest **62**: 202, 1956.
2. Kilpatrick, C.: High Speed in Amalgam Cavity Preparations, D. Digest **61**: 258, 1955.
3. Kilpatrick, C.: An Evaluation of Rotational High Speed and Coolant Equipment for Speed up to 200,000 R.P.M., Bull. Alabama Dent. A. **41**: 7, 1957.
4. Greene, Edward B.: Measurements of Human Behavior, New York, 1941, The Odyssey Press.

ANNOUNCEMENTS

European Organization for Research on Fluorine and Dental Caries Prevention

The sixth congress of the European Organization for Research on Fluorine and Dental Caries Prevention (ORCA) will take place in Pavia, Italy, July 3 to 5, 1959. The main theme of the congress will be "Caries Tests."

Dr. Rudolf Naujoks, Univ.—krankenhaus Eppendorf, Martinistr. 52, Hamburg 20, Germany, is preparing the scientific program. Prof. Dr. Silvio Palazzi, Corso d'Italia 49, Milano, Italy, is chairman of the organizing committee.

Additional details concerning the Congress will be announced later.

Second Symposium on Gnotobiotic Technology: The Rearing and Use of Germfree Animals

A national symposium on the technology of germfree research will be held Wednesday and Thursday, April 8 and 9, 1959, at Lobund Institute, University of Notre Dame, South Bend, Indiana.

Registration for the two-day symposium begins at 8 A.M., April 8, on the campus of the University of Notre Dame, and the first session is at 10 A.M.

Further information is available from Professor Philip C. Trexler, Lobund Institute, University of Notre Dame, South Bend, Indiana, and Donald L. Snow, Chief, Sanitary Engineering Branch, Division of Research Services, National Institutes of Health, Bethesda, Maryland.

First District Dental Society

A lecture entitled "Surgical Preparation of the Mouth for Dentures" will be given by Drs. Loscalzo and Pleasure at the meeting of the Section on Oral Surgery, First District Dental Society, at 8 P.M. on Wednesday, March 18, 1959, at Hotel Statler in New York City.

Lawrence Salman, Secretary
250 West 57th St.
New York 19, New York

International Academy of Oral Pathology

Through the gracious support of the Charles Ulrich and Josephine Bay Foundation, the International Academy of Oral Pathology will hold its first conference in New York City at the time of the centennial meeting of the American Dental Association.

The International Academy of Oral Pathology was founded by a group of internationally prominent oral pathologists. The founding fellows are Professor Robert V. Bradlaw of Durham University, England; Colonel Joseph L. Bernier of the Armed Forces Institute of Pathology, Washington, D. C.; Dr. Lester R. Cahn, Professor of Oral Pathology, Columbia University; Professor J. J. Pindborg of the University of Copenhagen; Dr. Reidar Sognnaes, formerly of Norway, now Brachet Professor of Oral Pathology at Harvard University; Professor Martin Rushton of Guy's Hospital, University of London; and Dr. Kurt H. Thoma, Professor Emeritus, Harvard University.

The program of the conference will be announced later. Included in this program will be the first of the Charles Ulrich and Josephine Bay Lectures.

The headquarters of the International Academy of Oral Pathology is at the Armed Forces Institute of Pathology in Washington, D. C.

Joseph L. Bernier
Colonel, DC, USA
Secretary

Academy of Dentistry for the Handicapped

The annual meeting will be held on Sunday, Feb. 8, 1959, at the Conrad Hilton Hotel in Chicago, Illinois, in conjunction with the midwinter meeting of the Chicago Dental Society.

Dr. Saul Levy, of the Department of Dentistry of Michael Reese Hospital, will address the Academy on "Dentistry for the Handicapped in Hospitals."

Dr. Boyd F. Sprague of Portland, Oregon, will speak on "Rectal Anesthesia for the Handicapped Patient."

Drs. Manuel M. Album of Jenkintown, Pennsylvania, and Hugh Kopel of Detroit, Michigan, will discuss "Drug Therapy and Dosage in Dentistry for Children."

Further information may be obtained by writing to the secretary, Dr. Robert I. Kaplan, 3038 Federal St., Camden 5, New Jersey.

University of Alabama

The School of Dentistry will present the following refresher courses during the months of April and May, 1959:

Partial Denture Prosthesis. April 3-5.
William L. McCracken

Oral Medicine. April 10-12.
Emanuel Cheraskin.

Immediate Root Canal Therapy Followed by Apicoectomy. May 7 and 8.
Adeeb E. Thomas.

Pedodontics for the General Practitioner. May 16 and 17.
Sidney B. Finn.

Anatomy of the Head and Neck. May 25-27.
Harry Sicher.

For further information, please contact the Director, Refresher Course Program, University of Alabama School of Dentistry, 1919 Seventh Ave. South, Birmingham, Alabama.

Boston University and Massachusetts Memorial Hospitals

The Department of Stomatology, Division of Graduate Studies, School of Medicine, Boston University, and the Massachusetts Memorial Hospitals announces the following postgraduate courses:

Advanced Course in Periodontal Therapy. Drs. Henry M. Goldman, Bernard S. Chaikin, and Staff. March 2-7, 1959. $250.00.

Technics in the General Practice of Dentistry. Staff. March 9-14, 1959. $175.00.

Periodontal Therapy. Drs. Henry M. Goldman, Bernard S. Chaikin, and Staff. March 16-27, 1959. $350.00.

Tooth Preparation and Elastic Impression Material Technics in Crown and Bridge. Dr. Arthur Kahn. March 30—April 1, 1959. $100.00.

Full Denture Prosthesis. Dr. Chester Landy. April 6-10, 1959. $150.00.

Occlusal Adjustment. Drs. Bernard S. Chaikin, Henry M. Goldman, and staff. April 27—May 1, 1959. $200.00.

Endodontics. Dr. Herbert Schilder. May 11-15, 1959. $175.00.

Periodontal Prosthesis. Drs. Leo Talkov and David J. Baraban. May 18-22, 1959. $200.00.

Surgical Technics Employed in Periodontal Therapy. Dr. Lewis Fox. May 25-29, 1959. $200.00.

Pulp Protection in Operative Dentistry. Dr. Harold Berk. June 4-6, 1959. $100.00.

Periodontal Pathology. Drs. Henry M. Goldman, Jack Bloom, and Staff. June 8-12, 1959. $250.00.

Detailed hour-by-hour rosters for the courses are available upon request.

For further information or for application blanks, apply to Director, Postgraduate Courses, Department of Stomatology, Massachusetts Memorial Hospitals, 750 Harrison Ave., Boston 18, Massachusetts.

Georgetown University

The School of Dentistry announces a course in intravenous anesthesia for the dental office (for oral surgeons only) which will be given Monday through Friday, March 9 to 13, 1959. Tuition will be $250.00, and the class will be limited to fifteen. The course will be under the direction of Drs. Harold Krogh of Washington, D. C., and Adrian O. Hubbell of Long Beach, California.

University of Kansas City

The following postgraduate courses which have been approved by the Director of the Academy of General Dentistry, will be given by the University of Kansas City in 1959:

Endodontics. Dr. Nygaard Ostby, Oslo, Norway. February 13 and 14. $50.00.

Oral Radiology. Dr. William Koch, St. Louis, Missouri. February 28. $25.00.

Complete Denture Prosthesis. Drs. P. M. Jones, C. G. Porter, H. Eversull, D. D. Krajicek, and J. B. Darnell. March 3 to 7. $100.00.

Symposium on Hospital Procedures. Drs. W. Hart, R. A. Allen, W. J. Carter, C. J. Brown, R. Friedrich (A.D.A.), and Mr. Moore. March 5. $25.00.

Oral Diagnosis and Oral Medicine. Dr. H. G. B. Robinson. March 5. $25.00.

Dentistry for Handicapped Children. Drs. J. E. Wells, A. E. Iwersen, W. J. Carter, and A. F. Lindquist. March 6. $25.00.

Periodontics. Dr. Frank Buebe, New York, New York. April 1 and 2. $50.00.

Cephalometrics. Dr. R. M. Ricketts, Pacific Palisades, California. May 6 to 8. $75.00.

Oral Surgery. Colonel R. B. Shira, Walter Reed Hospital, Washington, D. C. June 19 and 20. $50.00.

Materials in Dentistry. Dr. Gunnar Ryge, Milwaukee, Wisconsin. September 3 and 4. $50.00.

Preventive and Interceptive Orthodontics. Dr. Faustin N. Weber and associate, Memphis, Tennessee. October 14 to 16. $85.00.

Prosthetics. Dr. Bernard Jankelson, Seattle, Washington. November 4 to 6. $75.00.

University of Minnesota

The Division of Oral Pathology is one of the first schools to be granted a Fellowship in Clinical Oral Pathology by the American Cancer Society for the period of July 1, 1959, to June 30, 1960. This will pay the recipient $3,600.00 per annum, taxfree, and is renewable upon approval of the American Cancer Society.

A program of education has been synthesized to give the trainee advanced experience in both clinical and basic material in dermatology, dermatopathology, biostatistics, tumor pathology, advanced oral pathology, pediatrics, and metabolic and endocrine disorders. A wealth of clinical material is available within the University of Minnesota Medical Center.

Applicants must apply before Feb. 15, 1959, forwarding a curriculum vitae and academic record. Inquiries should be addressed to

Dr. Robert J. Gorlin,
Chairman, Oral Pathology,
School of Dentistry,
University of Minnesota,
Minneapolis 14, Minnesota.

Tufts University

A special postgraduate refresher course in periodontology, entitled "Recent Developments on the Histopathology of Periodontal Disease," will be offered April 18 and 19, 1959. The course will be given by Dr. Jens Waerhaug, Professor of Dentistry and Head of the Department of Periodontology, Norwegian State Dental School, Oslo, Norway. Tuition will be $40.00.

A special course will be given Sept. 21 to 23, 1959, during the centennial meeting of the American Dental Association and the meeting of the Federation Dentaire Internationale which will be held in New York City—one hour away from Boston. The course, entitled "Modern Concepts Regarding the Etiology, Diagnosis, and Treatment of Oral Disease," will be given by Colonel Joseph L. Bernier, Chief, Branch of Dental and Oral Pathology, Armed Forces Institute of Pathology, Washington, D. C. Tuition will be $75.00. (Special tuition can be arranged for dentists from outside North America.) In this course, Colonel Bernier will interpret diseases of the oral mucous membrane and osseous structures in terms of underlying microscopic tissue changes. The cellular and clinical changes produced by local and systemic influences will be explained. The criteria for the early diagnosis of malignancy in the oral cavity and adjacent structures will be described.

For further information and application, write to Division of Graduate and Postgraduate Studies, Tufts University School of Dental Medicine, 136 Harrison Ave., Boston 11, Massachusetts.

Tufts University

Tufts University School of Dental Medicine announces two graduate courses in oral surgery.

I. Three-Year Graduate Course in Oral Surgery in Conjunction With the Boston City Hospital. Dr. Richard G. Taylor, Professor and Chairman of the Department of Oral Surgery, Tufts University School of Dental Medicine, and Director of the Oral Surgery Department at the Boston City Hospital.

This is a three-year training program in oral surgery arranged for persons interested in preparing for specialization and certification by the American

Board of Oral Surgery. The first year is spent at Tufts University School of Dental Medicine and consists of study in basic and applied sciences. The second and third years are spent as intern and resident at the Boston City Hospital.

The oral surgery service at the Boston City Hospital offers outstanding opportunities for training in all phases of major and minor oral surgery. There are 400 house admissions annually, and 22,500 outpatients seen each year. One hundred fifty fracture cases are treated each year. The oral surgery service enjoys excellent cooperation with other departments. The service provides an average of 650 consultations to other departments throughout the year. Three months during the years are spent in the anesthesia department, where attention is given to training in endotracheal techniques. Interns and residents are required to attend regular lectures, conferences, and clinics at the hospital as part of their training.

Preparation for a graduate degree is not a necessary feature of this course. Research activity is encouraged, however, and interested candidates may include degree qualification as part of the three-year program. Dental school graduates who have a B.S. degree are eligible for the Master of Science Degree. Dental school graduates who do not have a bachelor's degree may apply for the Master of Dental Science degree.

Participants in the program will be accepted for three years. However, advancement from year to year is contingent upon the candidate's satisfactory performance. Tuition for the first year is $1,000.00. For the remaining two years, there is no tuition charge and the participants receive a stipend from the hospital.

II. One-Year Basic Science Course in Oral Surgery. This is a one-year course designed to meet the needs of persons desirous of fulfilling the requirements for certification by the American Board of Oral Surgery. It is devoted to the basic and applied science background necessary for surgical practice. The opportunity for clinical work in oral surgery is not included in the curriculum of this one-year course.

For further information and application, write to Division of Graduate and Postgraduate Studies, Tufts University School of Dental Medicine, 136 Harrison Ave., Boston 11, Massachusetts.

Manhattan General Hospital

A new Department of Dentistry has been founded at the Manhattan General Hospital in New York City in connection with the care of city welfare patients suffering from pulmonary diseases. This department intends to foster the clinical knowledge of the treatment of oral problems in patients suffering from diseases of pulmonary origin. The staff will carry on research work.

Appointments in the Department of Oral Surgery will be made as the need for additional staff develops.

REVIEWS OF THE LITERATURE

MALIGNANT ORAL TUMORS

Multicentric Carcinomas of the Oral Cavity. C. G. Moertel and E. L. Foss. Surg., Gynec. & Obst. **106**: 652, June, 1958.

"The concept of epithelial carcinoma originating from a single minute focus at a single instant in time has been seriously challenged in recent years."

Of 732 patients with proved oral cancer seen at the Mayo Clinic during the ten-year period from 1944 through 1953, a total of sixty-four, or 8.7 per cent, were found to have two or more discrete oral cancers.

Associated leukoplakia was found in 75 per cent of the patients with multiple oral lesions. An overwhelming majority of the patients were users of tobacco, particularly in the forms which expose the mouth to tobacco juices.

When oral cancer develops, all of the contiguous squamous mucous membrane must be considered as highly susceptible to future malignant change.

The importance of appropriate prophylactic measures and periodic checkups in patients with known oral cancer is stressed.

T. J. C.

A Study of the Etiological Factors in Cancer of the Mouth. E. L. Wynder, I. J. Bross, and R. M. Feldman. Cancer **10**: 1300, 1957.

Environmental factors play a role in the development of cancer in man.

This study is based upon 659 patients with cancer of the oral cavity; 543 of the patients were men.

Smoking, particularly cigar and pipe smoking, was found to be an important factor in the development of cancer of the oral cavity in men. In women cigarette smoking represented a factor. Other extrinsic factors were dental irritation and alcohol consumption.

It is recognized that intrinsic factors play a role, but at present they remain unknown.

T. J. C.